The New England
Journal of Medicine

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VOLUME 223 JULY 11, 1940 NUMBER 2

CESAREAN SECTION IN MASSACHUSETTS IN 1938*

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WHEN the Executive Committee of the Section on Obstetrics and Gynecology[1] reported at the annual meeting of the Massachusetts Medical Society in 1938 on the cesarean sections for 1937, we did not know that we should be asked to continue the study. Since that time the Massachusetts Department of Public Health has asked us to make this a five-year study. This report, therefore, is for the second year, 1938. Although members of the committee have examined the figures, I alone am responsible for the opinions expressed. The same questionnaire was used for this report as was used in the first year. The report follows closely that for 1937, in order that comparisons may be readily made.

The questionnaire was sent to 171 licensed maternity hospitals. Replies were received from all. Thirty-eight hospitals reported no cesarean sections for the year. These were all small hospitals not equipped to do such operations.

*Presented in abstract before the Obstetrical Society of Boston, November 21, 1939.

In Massachusetts in 1938 there were 62,382 live births and 1730 stillbirths, a total of 64,112. Of these, 50,888 were reported to us as occurring in hospitals. There were 2216 cesarean sections performed and 16 hysterotomies, a total of 2232 abdominal deliveries, or an incidence of 1 in 28.7. Table 1 gives a summary of the abdominal deliveries.

Table 2 gives the indications for the 16 hysterotomies. Serious cardiac disease was responsible for most of these. It is interesting to note that 2 hysterotomies were done because of the presence of multiple sclerosis, and in the analysis of indications for cesarean section (Table 5), 3 were done for the same disease. The single case of erythroblastosis in a previous pregnancy as an indication for hysterotomy needs explanation. It is a recognized fact that it recurs in about 80 per cent of pregnancies. This patient had previously had an erythroblastosis of the icterus gravis type, and following a consultation it was thought best to sterilize her. Therefore a hysterotomy with sterilization was done. The other indications need no comment.

Table 3 shows the types of anesthesia employed. As in the first report, nitrous oxide, oxygen and ether was by far the commonest anesthetic. The use of cyclopropane and spinal anesthesia has increased. Anesthesia was recorded

TABLE 1. *Summary of Abdominal Deliveries.*

OPERATION	NO. OF CASES	
Cesarean section		2216
Emergency	995	
Elective	1196	
Not reported	25	
Type of operation:		
Low	1206	
Classical	934	
Latzko	13	
Porro	25	
Peritoneal exclusion	1	
Not reported	37	
In labor	744	
Not in labor	1433	
Not reported	39	
Membranes ruptured	331	
Membranes unruptured	1807	
Not reported	78	
Hysterotomy		16
Total		2232

TABLE 2. *Indications for Hysterotomy.*

INDICATION	NO. OF CASES
Cardiac disease	7
Hypertension	2
Multiple sclerosis	2
Hydatidiform mole	1
Tuberculosis	1
Erythroblastosis in previous pregnancy	1
Fibroid uterus	1
Manic depressive insanity	1
Total	16

as the cause of death in 5 cases, all elective sections. They are reported below.

Table 4 shows the recorded indications for operation in the cases in which the babies died. There

TABLE 3. *Types of Anesthesia.*

ANESTHETIC	NO. OF CASES
Nitrous oxide, oxygen and ether	1533
Ether	260
Cyclopropane	159
Spinal	106
Nitrous oxide and oxygen	19
Avertin	29
Local	34
Other	50
Not reported	26
Total	2216

were 131 emergency cesarean sections in which the baby was lost, and 55 elective operations, with the loss of 56 babies, including one set of twins.

Why should 27 babies have been lost in elective cesarean sections done because of previous sections? Analysis of these deaths brings out some interesting points. In 6 cases the cause of death was recorded as prematurity. In 6 others it was pulmonary atelectasis. Were these patients oper-

TABLE 4. *Indications for Operation in Cases with Death of the Baby.*

INDICATION	EMERGENCY CESAREAN SECTION	ELECTIVE CESAREAN SECTION
Separated placenta	45	–
Placenta previa	29	2
Toxemia and nephritis	14	7
Previous cesarean section	7	27
Prolonged labor	12	–
Contracted pelvis	5	6
Ruptured uterus	6	–
Previous operative attempts	3	–
Desire of patient	–	3
Eclampsia	2	–
Test of labor	2	–
Previous disaster	–	2
Prolapsed cord	1	–
Double uterus	1	–
No progress	1	–
Multiparity	1	–
Cervical dystocia	1	–
Hydrocephalus	–	1
Previous vaginal operation	–	1
Ankylosis of hip	–	1
Advanced age and rigidity of cervix	–	1
Pyelitis	–	1
Chorea	–	1
Brain tumor	–	1
Thyrotoxicosis	–	1
Not reported	1	–
Totals	131	56

ated on too early? Was too much medication given the mother before operation? Six other babies were recorded as stillborn with no explanation. Three of them, however, were macerated, and 1 of these was an anencephalic infant. There were 2 monstrosities, 1 baby with congenital absence of the bile ducts and 1 with erythroblastosis. These last two conditions, of course, were totally unpredictable. One baby died of inanition in four weeks' time, and in 1 resuscitation failed. One each died of purpura of the newborn, intracranial hemorrhage and bronchopneumonia.

That 13 babies should be lost through prematurity and inability to establish respiration is a serious criticism. One of the reasons for doing a section on toxemic cases is to obtain a living baby, yet in 7 elective sections the baby was lost. That the babies were lost in 3 elective cesarean sections done because of the desire of the patient, is shocking. It is also inexcusable that 2 babies should have died after cesarean section done because of previous disasters, and it is hard to explain why 6 babies were lost when the indication was a contracted pelvis.

The other indications would be questionable if living babies had been obtained, but with the loss of the babies they are without justification.

In the emergency cases, it is not surprising that 45 babies died because of separated placenta. The percentage, 44 per cent, is to be expected with this complication. The question arises whether some of these mothers would not have been better delivered from below than by cesarean section. It is easy to understand why babies were lost following prolonged labor, ruptured uteri and previous operative attempts. Little need be said in regard to the deaths of babies in the other emergency sections. In some cases severe criticism is due the physician for choosing a section as the method of delivery.

Table 5 records the indications for cesarean section. As last year, the indications were various and bizarre. With the number of cesarean sections that are being done in Massachusetts, it is of course reasonable to have the indication of previous section lead the list. The next most frequent indication is disproportion. How many of these cases presented a disproportion sufficient to warrant a section, it is impossible to judge. However, one gets the impression that many sections done for this indication were unnecessary.

The number of cesarean sections done for separated placenta has increased decidedly. It is doubtful whether all were justified, for several patients were only six or seven months pregnant and undoubtedly could have been managed better from below, by rupturing the membranes and using the Spanish windlass.

The number of sections for toxemia and nephritis remains about the same. Were ideal prenatal care given all patients, undoubtedly the incidence would be lower. That it should seem essential to do 125 sections for these conditions shows a total lack of co-operation on the part of the patient and of careful, intelligent treatment by the physician.

Malposition of the baby as an indication needs little comment, except that it seems that cesarean section is being done with increasing frequency for breech presentations.

Under the grouping "Dystocia" there were 202 cases. There has apparently been a greater attempt to allow a test of labor than appeared from the first report. Whether or not this is simply a slight change in the way the questionnaires were answered, it is difficult to say. Sixty sections were done for cervical dystocia and uterine inertia, but when it appears that patient after patient had only a few hours of labor, often reported as mild or poor, one cannot help wondering whether all these sections were necessary.

It is impossible to evaluate accurately the next group of cases, "Previous surgical operations." It is, however, fair to make a few comments. A simple repair of the perineum or of the cervix cannot always be said to be an adequate indication, while after amputation of the cervix, section is the conservative procedure. Suspension of the uterus should seldom call for a subsequent section.

The other indications under this group need little explanation. The criterion for decision in regard to previous myomectomies, I think, is the size, position and number of scars in the uterine wall. As these are unknown, the indication must be accepted as valid. In the case of a previous gastroenterostomy, it was thought that a section would be the best way out of a serious complication. The justification for a section because of a goiter operation five months before term is probably questionable. In the nephrectomy cases both patients showed severe toxemia.

Under "Associated medical conditions," cardiac disease leads the list. There is no way of judging whether all the cases should have had sections. Many cardiac patients, especially multiparas, have a surprisingly easy labor, and there is not the risk of distention that might follow a section.

This year it happened that 9 diabetic patients had sections. The explanation is that these women were under the care of physicians who believed that many such cases are better managed by a section than by allowing the patient to go through labor. There are in Boston two totally different schools of thought in the management of diabetic cases.

TABLE 5. *Indications for Cesarean Section.*

Indication	No. of Cases
Previous section	635
Contracted pelvis and disproportion	477
Placenta previa	175
Separated placenta	104
Toxemia and nephritis	125
Eclampsia	9
Malposition of baby	110
Breech	78
Transverse	22
Brow	1
Shoulder	2
Face	5
Prolapse of hand	1
Compound malposition	1
Dystocia	202
Dystocia	28
Labor without progress	47
Test of labor	60
Cervical dystocia	30
Uterine inertia	30
Persistent ODP	6
Contraction ring	1
Previous surgical operations	43
Repair of perineum	24
Amputation of cervix	6
Repair of cervix	1
Suspension of uterus	3
Myomectomy	4
Vaginal operations	1
Gastroenterostomy	1
Thyroidectomy (5 months before)	1
Nephrectomy	2
Associated medical conditions	61
Cardiac disease	31
Tuberculosis	5
Diabetes	9
Bronchiectasis	1
Epilepsy	1
Chorea	1
Fragilitas ossificans	1
Multiple sclerosis	3
Psychosis	2
Arthritis	2
Pyelitis	2
Brain tumor	2
Hypothyroidism	1
Previous obstetric disaster	47
Elderly primipara	70
Obstructing tumors (fibroids)	18
Fetal distress	7
Prolapsed cord	3
Following operative attempts	7
By request or for sterilization	17
Request	6
Sterilization	11
Ruptured uterus	8
Spontaneous	1
Previous section	7
Injury or disease of pelvis	6
Bicornate uterus	3
Postmaturity	4
Social and economic reasons	3
Varicosities of vagina	2
Congenital dislocation of femur	1
Malformation of fetus	1
Abdominal hernia	1
Obesity	1
Malformation of vagina	1
Desire for live baby	1
Frequent miscarriages	1
Bizarre	25
Twins — 3 with locked heads	5
Pain in right hip	1
"From history, cesarean section best"	1
Elderly multipara	1
Multiparity	1
High nervous state of mother	1
Fetal dystocia	1
"Pelvic findings indicate cesarean section"	1
Threatened placenta previa	1
Maternal debility	1
Braxton-Hicks contractions	1
Pregnancy at term	3
Unengaged head	4
Rupture of membranes and no labor	1
Length of ruptured membranes	1
"Right occiput transverse by x-ray"	1
Not reported	48
Total	2216

Previous obstetric disaster may or may not be a proper indication. Each case of this type must be carefully studied and the decision must depend on the individual case. The mere fact that a woman has had one disaster is not an absolute indication for a cesarean section in the next pregnancy.

Again, the fact that the patient happens to be an elderly primigravida is not in itself an indication for a section. Each case requires individual study before a reasonable and sane decision can be made.

A cesarean section done because of fetal distress resulting in a stillborn baby is a dubious procedure. It is equally questionable to do one because of fetal distress, and have the baby cry just as it is being born.

Subjecting a woman to a cesarean section because of a prolapsed cord undoubtedly is justifiable in some cases, but the decision requires careful judgment.

TABLE 6. *Summary of 60 Cases with Maternal Death.*

DATA	NO. OF CASES
Emergency operation	39
Elective operation	21
Not reported	0
Type of operation:	
Low	26
Classical	24
Porro	3
Through rupture	2
Not reported	5
In labor	25
Not in labor	30
Not reported	5
Membranes ruptured	18
Membranes unruptured	37
Not reported	5
Babies:	
Living	43
Dead	17

The seriousness of doing a section after operative attempts is shown by the fact that of the 7 cases in which that indication was given, 4 mothers and 4 babies were lost.

I cannot bring myself to accept the request of the patient as a reasonable indication for a section. Nor do I believe that cesarean section for the purpose of sterilization is good practice. In my opinion it is much safer to allow the patient to have a normal delivery, and if sterilization is indicated to do it at a later time.

Of the 8 cases of ruptured uterus, 1 was spontaneous and 7 were the result of previous cesarean sections. That, of course, is what we must expect with the increasing incidence of cesarean section.

It is understandable that there might be so severe an injury to or disease of the pelvic bones that a cesarean section would be indicated. But the fact that the patient has had such an injury is not itself an indication for one. The criterion is whether the pelvis has been so narrowed that a delivery cannot be safely accomplished.

I have grouped as bizarre indications those given for 25 sections. Others could readily be placed in this group. There is no need to comment on each of these. It is apparent to any thoughtful observer that they are not good and sound reasons for subjecting a woman to a major operation.

In 1938 there were, as I have already reported, 2232 abdominal deliveries with 60 maternal deaths, giving a maternal mortality rate of 2.7 per cent. This is an excellent result, a little lower than that of 1937, which was 3.1 per cent.

No comment need be made on Table 6, as it is simply an analysis of the operations where death of the patient followed.

In Figures 1 and 2, the data are presented in a different manner from similar data in the first report. They show more clearly the indications for operation and the causes of death in the 60 cases with fatal results. Figure 1 analyzes the 21 elective sections and Figure 2 the 39 emergency operations in which death occurred. I have already spoken of many of the indications, and there is no need of making further comment on these. But the causes of death in the 21 elective sections must be analyzed.

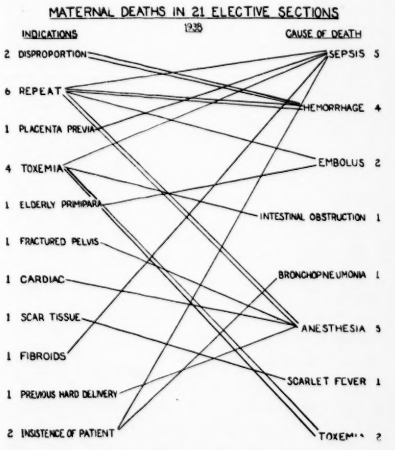

FIGURE 1.

That 5 patients died of sepsis makes it clear that obstetricians and surgeons must be more careful in their operative technic. The same is true of hemorrhage. There should not have been 4 deaths

from this cause. The 2 deaths from pulmonary embolus cannot be regarded as preventable. In the death that took place from intestinal obstruction, the patient was operated on three days after the original operation, and the obstruction was freed, but she failed to survive the second operation.

Whether the death from bronchopneumonia can be considered an anesthetic death is question-

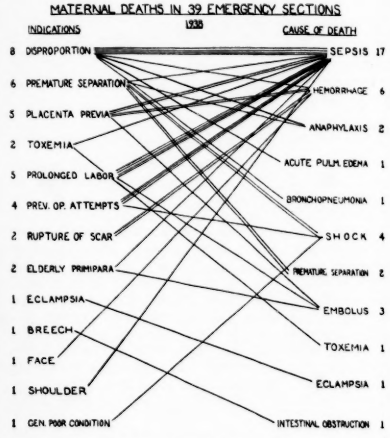

FIGURE 2.

able. There are, however, 5 deaths that were attributed to anesthesia. One patient, while she was going under ether, had a severe choking spell, followed by massive collapse of the lung and death. In the second case a spinal anesthetic was used. The patient died at once, and the autopsy showed that there was some cardiac complication. Whether or this is a true anesthetic death is debatable. The third case was that of a woman who had had severe attacks of asthma and had great difficulty in the first stage of anesthesia. This, I think, can be definitely regarded as death from anesthesia. In the fourth case again there was difficulty in giving the anesthetic and the patient died before the operation was completed. The last case was similar. There was considerable difficulty in the induction of anesthesia, and in twenty-four hours the patient developed pneumonia. In this case, even though the anesthesia went badly, the operation was prolonged in order to do a sterilization and an appendectomy. It would seem poor judgment to subject the patient to so much operative work when the anesthesia was going badly.

The death from scarlet fever can hardly be regarded as preventable. The 2 deaths from toxemia show that there had been inefficient prenatal care, and the choice of cesarean section was unwise.

Figure 2, which gives the indications and causes of death in the 39 emergency sections, demonstrates the seriousness of doing emergency sections in cases not properly prepared. Seventeen of these women died from sepsis. It is not necessary to mention each indication, but it should be noted that of the 5 patients whose labor was prolonged, 4 died of sepsis. There were 4 deaths following previous operative attempts, 3 from sepsis and 1 from shock, the patient not living long enough to develop sepsis.

Again this year we have deaths from anaphylaxis. This suggests that the technic in the matching of blood must be perfect, or serious reactions with death will follow.

The patient who died of acute pulmonary edema was badly managed outside the hospital, and she was in very poor condition on entrance. In spite of proper treatment after entrance, death followed.

Whether the cases classed under premature separation are correctly assigned is uncertain. There was, however, no marked hemorrhage. There was not enough evidence to assign the cause to toxic separation, so I have left the cause of death as given. The number of cases of eclampsia is again low, as already reported, but 1 woman died.

The last case, one of intestinal obstruction, had an emergency operation for a primiparous breech. The patient had marked distention and a rise in temperature immediately after the operation. The death certificate gave mesenteric thrombosis with intestinal obstruction as the cause of death. Whether this is correct or whether the cause was sepsis, there is no way of telling, as there was no autopsy.

In analyzing these deaths, both elective and emergency, it is fair to say that the number of deaths from sepsis should have been lower. There were other obviously preventable deaths. Exactly how many, it is difficult to say. The fact that deaths from anaphylaxis and from poorly administered anesthesia are still occurring is a serious criticism of the profession. These deaths must be eliminated.

This year we have made no attempt to appraise the number of consultations that were held, for the questionnaires were vague and gave us no basis on which to work. I repeat what I said in my first report: I am confident that if the American College of Surgeons should withhold its approval from hospitals where no obstetric consultations are held, the number of cesarean sections would be materially diminished.

The results from these cesarean sections throughout the State are excellent. But too many are being done, and the deaths from them are unquestionably a factor in the maternal mortality rate for the State. Cesarean sections figured in something over 20 per cent of all maternal deaths. It should be the aim of all physicians to reduce the number of unnecessary cesarean sections, thereby eliminating some of the preventable maternal deaths and lowering the maternal death rate.

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REFERENCE

1. DeNormandie, R. L.: Cesarean section in Massachusetts in 1937. *New Eng. J. Med.* 219:865-871, 1938.

HIATUS HERNIA SIMULATING CARDIAC INFARCTION*

Report of a Case

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HERNIA of the stomach through the esophageal opening in the diaphragm may be asymptomatic or may simulate a variety of other conditions, one of which is cardiac infarction. Examination of recent textbooks discloses that hiatus hernia is given scant description, or none at all. The delay and confusion in achieving the correct diagnosis have prompted the report of a case of hiatus hernia, a review of the recent literature, a description of the symptoms and an analysis of a group of patients diagnosed at the Massachusetts Memorial Hospitals.

CASE REPORT

The patient was a 52-year-old physician, whose chief complaint was pain under the sternum and in the left arm, which woke him at 3 a.m. on December 8, 1937. He was seen by a cardiologist 5 hours later.

The pain was persistent and not completely abolished by two ¼-gr. doses of morphine. Occasional pain, of moderate severity, was noted at the inner aspect of each elbow and in the little finger of each hand. The left-sided pain predominated and the arm pains were estimated to last for 1 to 3 minutes at a time. The patient recognized little if any pressure symptoms and did not feel particularly ill. Gastric symptoms were absent.

During the subsequent 4 days he remained in bed. The white-cell count remained normal, fever was absent, electrocardiograms were normal, and the examination of the heart gave normal findings. The substernal discomfort was localized under the lower third of the sternum, where it persisted in a mild form. The patient was discharged at the end of 4 days as not having cardiac infarction, but with "something wrong in the mechanics of the chest."

The patient did not feel well during subsequent weeks. The above symptoms persisted in a mild form, and occasionally, in association with nervous tension, pain at the point of the left elbow reappeared and persisted for 3 to 15 minutes. The patient reported a sensation similar to that felt when one swallows something too hot. A roentgen examination, which unfortunately did not include search for a hiatus hernia, disclosed nothing abnormal in the esophagus and gastrointestinal tract.

A vacation of 6 weeks in Florida was prescribed. He was able to play golf, but there was only slight lessening of the thoracic and arm pain. In April, 1938, the patient consulted an orthopedic surgeon who previously had successfully treated him for certain postural defects. Delay in consulting an orthopedist was in part due to the fact that the patient wished to become more certain that coronary disease was not present. The orthopedist thought that if the substernal pain was not due to cardiac disease, it could be explained on the basis of muscular strain from faulty posture. Exercises were prescribed. These were faithfully followed until September without relief of the symptoms.

On June 19 an attack similar to that of the previous December occurred. A different cardiologist was called and he, after 2 days' study of the patient as a bed case, was satisfied that cardiac infarction was not present. The symptoms were believed to be partly orthopedic, partly cardiac and partly gastric in origin.

During the summer the patient resumed active exercise without untoward symptoms. Such exertions as running an eighth of a mile, baseball and tennis for several hours did not induce symptoms. The substernal and arm pains were present with increasing frequency at other times. Finally it was noted that the pain was tending to center under the lower third of the sternum and that the raising of gas and feeling of discomfort after meals were becoming more frequent. Smoking was reduced, and omitted entirely for periods of 2 or 3 weeks. The patient thought that a gastric disturbance might be present, but obtained no relief by the taking of alkalis or the ingestion of milk, crackers and so forth. A weekly diary of the symptoms made it apparent that they were increasing in frequency, but so variable in character that their causation remained obscure. It was noted that within a few moments of going to bed the substernal and occasionally the arm pain reappeared. For lack of a better explanation the patient was forced to consider his condition a functional neurosis, although he suspected that "undiagnosed" was a possibility.

It was decided to consult a gastroenterologist. Accordingly, Dr. Chester M. Jones, of Boston, was consulted in September, 1938. He suggested the diagnosis of a small hernia of the stomach at the esophageal hiatus of the diaphragm. The hernia was demonstrated both fluoroscopically and on a roentgen plate.

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The establishment of the diagnosis was of decided value to the morale of the patient. Medical treatment for some months was of uncertain benefit. In May, 1939, he consulted Dr. Stuart W. Harrington, of the Mayo Clinic, regarding surgical repair of the hernia. The hernia at this time could not be detected radiographically, but esophagoscopic examination disclosed reddening of the mucosa of the lower end of the esophagus and a few erosions on the gastric side of the esophagogastric junction. Dilation of the esophagus was performed. Radical cure by surgery was deemed unwarranted. The patient concurred with Dr. Harrington's judgment. There was a gradual abatement of symptoms to the date of writing, January, 1940; whatever symptoms occurred were minor and readily ignored. No treatment was followed save greater regularity in mealtime, and avoidance of large meals, exertion that put pressure on the abdomen, and nervous tension.

Recent Literature

Hernia of the stomach at the esophageal hiatus is described mostly in the surgical literature. Among the articles are those of Moersch,[1] reporting 246 cases; Harrington,[2] 416 cases; and Morton,[3] 46 cases among 56 patients with all types of diaphragmatic hernia. Unfortunately, information pertaining to herniation at the esophageal opening is often mixed in with that concerning other types of diaphragmatic hernia, and the latter, often larger and more spectacular, are given the fuller description of the two.

The strictly medical literature contains but little mention of the hiatus type of hernia and its simulation of coronary disease.[4] A good description, however, is among the recent additions to *Nelson's New Loose-Leaf Medicine*[5]; it credits Friedenwald and Felderman in 1925 with the first description of hiatus hernia and its mode of detection. Herrick[4] mentions a case in which he finally demonstrated that an esophageal hiatus hernia was present, but states somewhat facetiously that the patient, a physician, still prefers his own original diagnosis of coronary disease. Perhaps this conveys a suggestion that the simulation of coronary disease by hiatus hernia of the diaphragm is often foreign to medical thinking.

Frequency and Symptomatology

French[6] states that hiatus hernia is a very rare condition. However, its more frequent occurrence seems probable from the literature cited above, and particularly from Harrington's[2] report of 416 cases diagnosed at the Mayo Clinic. The first case in this group was demonstrated at operation in 1908; the first to be diagnosed roentgenologically was encountered in 1921. From 1908 to 1926 there were 17 such cases; from 1927 to 1938 the number rose to 399. Only 1 case was diagnosed roentgenologically in 1927, as contrasted with 92 in 1937. Although hiatus hernias are considered to be congenital in origin, the average age at which patients in this series experienced symptoms which caused them to consult physicians was in the decade of fifty to fifty-nine.

Some of the salient points, found mostly in Harrington's comprehensive article, may profitably be repeated here. The symptoms vary from none to complete disability. Although their severity tends to correspond to the size of the hernia, it has been found that many small hernias cause severe symptoms.

Hiatus hernia has been termed the "masquerader of the upper abdomen." An average of three erroneous clinical diagnoses in each case in the series preceded the final recognition of the hernia. Harrington lists these in the order of their frequency as cholecystitis, cholelithiasis, gastric ulcer, duodenal ulcer, hyperacidity, secondary anemia, cardiac disease, carcinoma of the cardia, stricture of the esophagus, appendicitis and intestinal obstruction. Twenty-one patients had been subjected to operation for other conditions without benefit, but were promptly relieved when the hernia was repaired.

The chief symptoms are pain, gaseous eructation, vomiting, dyspnea, hemorrhage, weakness, anemia and cardiac palpitation. They are usually mild at first. The first symptom is often pain projected through to the back, during or shortly after a meal. This pain may follow the ingestion of any substance, even a cup of coffee, into an empty stomach. It is relieved by belching or vomiting. The pain is felt more on the left side of the back and often between the scapulas. It is frequently associated with phrenic pain, and may radiate down the left arm, as in coronary disease.

The pain may be worse on lying down, and the patient may find relief by resuming an upright posture. The pain varies in duration from a few minutes to several hours. It shows no constant relation to physical exertion. There may be intermissions of weeks or months between attacks. When the distress has become constant, the stomach is usually found to be fixed above the diaphragm by adhesions.

A loss of weight from the reduction of food intake due to "food fear" may occur. It has also been noted that the taking of a restricted amount of food at frequent intervals, under the erroneous diagnosis of gastric ulcer, may lessen the symptoms. Hemorrhage is uncommon, but gastritis

and even an ulceration in the herniated portion of the stomach have been found.

Assuming an upright posture may cause the hernia to be reduced. It is for this reason that the technic of roentgen-ray examination for the detection of such hernias requires that the patient be examined in the horizontal and even the Trendelenburg position before the presence of a hiatus hernia can be excluded. It is advantageous in suitable cases to exert upward pressure by palpation deep in the epigastrium during fluoroscopic study. The use of barium is, of course, part of the technic.

Massachusetts Memorial Hospitals Cases

Twelve patients seen in this hospital from 1931 to 1937 were found to have hiatus hernia.* The hernia was demonstrated in 1 case during a laparotomy and in the others by roentgen examination. The average age was fifty-eight, and the age range forty-three to seventy-six.

None of these cases were diagnosed correctly prior to admission, and their records contain little evidence that a correct clinical diagnosis preceded the finding of the hiatus hernia during roentgen-ray examination of the stomach. One patient had apparently been diagnosed erroneously, at the time of a prior admission to another Boston hospital, as suffering from cardiac infarction.

The duration of the symptoms believed to be due to the hernia was four months in 2 cases and varied from one to ten years in the remaining 10. Pain was the outstanding symptom, occurring in 9 cases; in 5 the symptoms resembled those of coronary disease; while in 7 they suggested gastric disease.

The relation to posture was very definite in 4 cases. This means that the symptoms were prone to occur or to increase when the patient lay down.

This group of patients complained of a multiplicity of symptoms such as were described by Harrington[2] and in the preceding case report.

Discussion

The case history given above illustrates a much-delayed diagnosis; a hiatus hernia was not thought of by the patient and the group of physicians consulted. I did recall an obscure case reported by Levine[7] in which an ulcer of the esophagus was finally disclosed as the cause of a simulation of angina pectoris. Roentgen-ray study in January, 1938, however, disclosed nothing abnormal in the esophagus; it was not realized at the time that normal roentgen-ray findings do not exclude esophagitis. The significance of the increase in symptoms on assuming the recumbent posture was appreciated only subsequent to the diagnosis of hiatus hernia.

There is a difference of opinion regarding the need for surgical intervention. Crushing of the phrenic nerve, judging from reports in the literature,[8] is of doubtful value. Medical treatment may sufficiently relieve some patients whose hernias appear to cause symptoms; if not, radical repair warrants consideration. Description of the operation discloses that it is a major surgical procedure. Harrington selected 102 of his 416 cases of hiatus hernia for surgical repair, and the results were highly successful.

*A larger number appear in the records of the Roentgen Department.

Summary and Conclusions

A case report of a patient with an esophageal hiatus hernia of the diaphragm is presented. Coronary thrombosis was simulated, and the correct diagnosis was much delayed.

A brief review of the recent literature and a description of the symptoms are offered.

A group of cases diagnosed at the Massachusetts Memorial Hospitals is included.

Hiatus hernia may simulate cardiac infarction as well as a group of gastric and abdominal diseases.

Hiatus hernia should become a more frequent diagnostic possibility in the differential diagnosis of certain cardiac and upper-abdominal diseases.

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References

1. Moersch, H. J.: Hiatal hernia. *Ann. Otol., Rhin. & Laryng.* 47:754-767, 1938.
2. Harrington, S. W.: Esophageal hiatus diaphragmatic hernia: etiology, diagnosis, and treatment in one hundred and twenty-three cases. *J. Thoracic Surg.* 8:127-149, 1938.
3. Morton, J. J.: Herniation through the diaphragm. *Surg., Gynec. & Obst.* 68:257-277, 1939.
4. Herrick, J. B.: On mistaking other diseases for acute coronary thrombosis. *Ann. Int. Med.* 11:2079-2085, 1938.
   Bean, W. B.: Infarction of the heart: symptomatology of acute attack. *Ann. Int. Med.* 11:2086-2108, 1938.
   Levine, S. A.: Angina pectoris and its relation to coronary artery disease. *New Eng. J. Med.* 219:743-746, 1938.
   Ballinger, W. M.: Low chest and upper abdominal pain. *Ann. Int. Med.* 12:1223-1232, 1939.
5. Eusterman, G. B.: Visceroptosis and hernia. *Nelson's New Loose-Leaf Medicine.* Vol. V. New York: Thomas Nelson & Sons, 1935. P. 336.
6. *An Index of Differential Diagnosis of Main Symptoms.* Edited by H. French. Fifth edition. 1145 pp. Baltimore: William Wood & Co., 1936. P. 794.
7. Levine, S. A.: A case of ulcer of the esophagus with extraordinary medical experiences. *Med. Clin. North America* 13:189-195, 1929.
8. Graham, E. A.; Singer, J. J., and Ballon, H. C.: *Surgical Diseases of the Chest.* 1070 pp. Philadelphia: Lea & Febiger, 1935. P. 473.

A LARGE ADENOFIBROMA OF THE BREAST

Report of a Case

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A TUMOR of the breast allowed to grow until it weighs nearly 25 pounds is a curiosity. The purpose of this paper is to describe a case of an adenofibroma of the breast which weighed 24.6 pounds (11.2 kilograms). This is the largest tumor of this type that has been reported with a pathological description and a photomicrograph. Cheatle and Cutler[1] in their monograph on tumors of the breast mention only one fibroadenoma of the breast larger than this. It was reported by Gross and weighed 29 pounds. A perusal of the 25 articles published since 1930 that mention large breast tumors reveals very few of comparable size.

The tumor of the breast most likely to grow to tremendous proportions is the giant intracanalicular myxoma. This condition has been thoroughly reviewed by Lee and Pack,[2, 3] who analyzed 109 cases. The average weight was 7.6 pounds. The only reference to extremely large tumors is von Graefe's in 1838 of one weighing 22.5 pounds, Desplats's report of one measuring 40 by 40 cm. and Ribbert's remark that such tumors may weigh as much as 20 kilograms. Martin[4] reported a breast tumor in 1933 in a sixteen-year-old Negress which weighed 33.3 pounds. The microscopic examination showed diffuse myxomatous degeneration and the diagnosis was giant lipofibromyxoma, so that Martin's case belongs in the myxoma group.

Only one extremely large fibroadenoma has been reported during the last decade. MacKenzie,[5] of Auckland, New Zealand, mentions a thirty-four-year-old woman with a breast tumor of two years' duration with ulceration of three weeks' duration and weighing 35 pounds. The diagnosis was fibroadenoma, but no microscopical description is given. Crile[6] discusses large bilateral adenofibromas of the breast and reports a thirteen-year-old girl with a tumor of the left breast that weighed 8.0 pounds (3.65 kilograms) and one of the right that weighed 4.7 pounds (2.12 kilograms). He states that the largest fibroadenomatous hypertrophy of the female breast that he found in the literature was that of Touraine and Renault.[7] This was a bilateral tumor consisting mostly of fat. The maximum circumference was 54 cm. and the combined weight of both breasts was 20.1 pounds (9.15 kilograms).

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CASE REPORT

C. F. S. (No. 1344), a 52-year-old woman, was admitted to the Cancer Section, Westfield State Sanatorium. She had first noticed a lump in the right breast 7 years previously. At that time she consulted a physician, who advised observation. The tumor had steadily grown. Three months previously the breast had started to ulcerate. She saw a physician 2 days before admission and was immediately referred to the hospital. She gave as her reason for the 7 years' delay that she feared the growth might be a cancer. The past history was irrelevant. The menopause had occurred 1 year previously. The patient had had one child but had not nursed it.

Examination was essentially negative except for the large

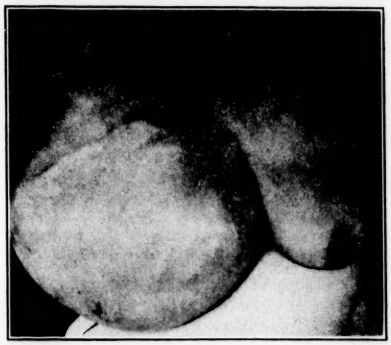

FIGURE 1.

right breast, which measured 35 by 30 by 28 cm. (Fig. 1). It was firm and irregularly nodular. There were several ulcerations, chiefly on the lateral and posterior portions, measuring up to 6 cm. in diameter. There were no enlarged axillary nodes. Biopsy of an ulcerated area showed adenofibroma. The blood pressure was 152/72. The significant laboratory findings were as follows: urinary albumin +; red-cell count 4,040,000, white-cell count 19,900, hemoglobin 81 per cent; sedimentation rate 124 mm. per hour (uncorrected Westergren); nonprotein nitrogen 31 mg. per 100 cc.; serum albumin-globulin ratio 0.9:1:0, total protein 6.2 gm. per 100 cc. X-ray films of the chest, skull, spine, pelvis and upper femurs were negative except for arthritis of the hip joints.

A simple mastectomy was performed on the 4th day under nitrous oxide, oxygen and ether anesthesia. The ulcerated areas were painted with collodion and covered with gauze. The tumor gave the gross appearance of invading the pectoralis major muscle, so a portion of the muscle was removed. There was also an extension of tumor beneath the upper portion of this muscle. A frozen section showed no evidence of malignant disease. A trans-

fusion of 500 cc. of citrated blood was given after completion of the operation. Convalescence was uneventful.

The pathological examination was made by Dr. Robert Fienberg, who reported as follows:

Gross Examination. The breast is greatly enlarged and nodular, forming a mass weighing 11.16 kilograms and measuring 40 by 30 by 20 cm. Ulcers are present in the skin, measuring 2.0 to 6.0 cm. in diameter, the largest being necrotic, black and malodorous. Dilated veins run through the skin. The inferior surface of the dissection is lobulated, yellowish-red and partly encapsulated by thick fibrous tissue. Masses of striated muscle are attached to this inferior surface and are partly incorporated in the fibrous tissue, thus giving the appearance of invasion of the striated muscle by the neoplasm. The sectioned surface of the breast reveals almost complete replacement by a huge edematous, encapsulated, lobulated neoplasm with only remnants of compressed breast at the periphery. The lobulations are of varied size and divided by thin strands of fibrous tissue. The neoplasm is grayish yellow, with large regions of reddish-brown necrosis.

FIGURE 2.

Microscopic Examination. The neoplasm consists of acini of various sizes lined by simple and pseudostratified cuboidal to columnar cells. There are a few papillary structures in wide acini and occasional mitotic figures in the epithelial cells (Fig. 2). The stroma about most of the acini is myxomatous, with dense connective tissue beyond the myxomatous region. The cellularity of the stroma varies moderately. The presence of mitotic figures indicates that the tumor was actively growing and suggests that it was still under hormonal influence in spite of the reported menopause one year previously.

Diagnosis: adenofibroma.

SUMMARY

A case of adenofibroma of the breast weighing nearly 25 pounds (11.16 kilograms) is reported. This is the largest adenofibroma of the breast that has been reported with pathological description and a photomicrograph.

REFERENCES

1. Cheatle, G. L., and Cutler, M.: *Tumours of the Breast: Their pathology, symptoms, diagnosis and treatment.* 596 pp. Philadelphia: J. B. Lippincott Co., 1931. P. 488.
2. Lee, B. J., and Pack, G. T.: Giant intracanalicular myxoma of the breast: the so-called cystosarcoma phyllodes mammae of Johannes Mueller. *Ann. Surg.* **93**:250-268, 1931.
3. *Idem:* Giant intracanalicular fibro-adenomyxoma of the breast: so-called cystosarcoma phyllodes mammae of Johannes Mueller. *Am. J. Cancer* **15**:2583-2609, 1931.
4. Martin, W. F.: Giant tumor of the breast. *South. M. J.* **26**:822, 1933.
5. MacKenzie, K.: A huge fibro-adenoma of the breast. *Brit. J. Surg.* **23**:234, 1935.
6. Crile, G., Jr.: Large bilateral adenofibromas of the breast: report of case in girl 13 years of age. *Surgery* **3**:68-74, 1938.
7. Touraine, A., and Renault, P.: Hypertrophie massive des seins sur fibro-adénome. *Bull. Soc. franç. de dermat. et syph.* **42**:300-302, 1935.

THE TREATMENT OF APPENDICITIS AT THE BURBANK HOSPITAL, FITCHBURG, MASSACHUSETTS*

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THREE years ago an outline of principles for the treatment of appendicitis was adopted at the Burbank Hospital in Fitchburg, Massachusetts. This report is an inventory of the subsequent results of this work on one of the two surgical services.

Fitchburg is an industrial city of approximately 40,000 people, surrounded by a considerable rural population. The hospital has 236 beds, of which 86 are ward beds. The ward surgery is managed by two services, each having a chief and two surgeons. The reorganization of the staff and all the work on appendicitis has been done under the direction of two Boston surgeons, and we have frequently had their assistance by telephone, by consultation and at operation. One surgical service is on duty in alternate periods of three months, and all members of the staff, besides carrying on this surgical work, are in general practice.

The principles we have adopted in managing appendicitis fall into three groups,— preoperative, operative and postoperative, — as follows:

Preoperative Treatment. The relief of dehydration and shock and the decompression of distention are done before operation whenever indicated. Many patients have been admitted to the hospital in a state of shock and dehydration. The administration of intravenous solutions by the constant drip method is begun immediately, and continued until the patient's condition has improved to the point where operation is thought advisable. This treatment is continued throughout operation and into the postoperative period. In cases with symptoms of peritonitis with distention, the use of a Levine tube with constant Wangensteen suction is immediately begun. The tube is left in for the operation, and as long after it as is considered necessary. It is remarkable how rapidly the condition of these patients improves in a few hours with this management.

Operative Treatment. There are two anesthetists on the ward surgical service, both of whom have had postgraduate study in anesthesia and are devoting most of their time to anesthesia. We believe that their excellent anesthesias have contributed greatly to our good results. We have used spinal anesthesia as often as was possible, otherwise nitrous oxide, oxygen and ether.

A right-rectus, muscle-retracting incision is used in almost every case. In 1 case a McBurney incision was used for the drainage of a palpable abscess. An attempt is made to remove all appendices under direct vision through adequate incisions. The general peritoneal cavity is carefully walled off before any attempt is made to touch the appendix, and suction is used whenever pus is present. Gentleness is constantly stressed. Whenever drains are necessary they are placed to the right of the cecum if possible, and are not removed before the seventh postoperative day. At the completion of the operation, when possible, the omentum is pulled down over the operative site. Appendectomy is done as soon as the diagnosis of acute appendicitis has been made or as soon thereafter as the patient's condition warrants. The base of the appendix is tied with two ties, without crushing. The stump is cauterized with carbolic acid, followed by alcohol, but is not inverted.

Postoperative Treatment. Clean cases are allowed liquids if there is no nausea or vomiting; in the others, fluids are maintained by intravenous solutions, following the plan of Coller, Dick and Maddock.[1] Cases with drainage are put in Fowler's position and given nothing by mouth or rectum, adequate fluids, and enough morphine to keep them comfortable and quiet. Cases with general peritonitis are put on Wangensteen drainage.

The cases of appendicitis have been divided into three groups: acute appendicitis, where the symptoms and signs were acute, regardless of the pathological findings; recurrent or chronic appendicitis, where there was a history of repeated attacks of pain and where the appendix was reported by the pathologist as showing "healed appendicitis" (routine appendectomies done at the time of other operations were not included); and acute appendicitis with perforation and abscess formation, spreading peritonitis or generalized peritonitis.

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The total number of cases treated was 172. There were 3 deaths, a mortality rate of 1.7 per cent. The mortality was confined to the third group mentioned.

There were 101 cases of acute appendicitis. Appendectomy was done in all cases except 1. This case occurred in a man of seventy-three, with extreme debility, chronic myocarditis and chronic nephritis. There were definite signs and symptoms of acute appendicitis. These disappeared under treatment and the patient recovered, dying three months later of cardiorenal disease. Two cases were complicated by early pregnancy; both patients recovered following appendectomy and went to full-term delivery. There was 1 case in which appendectomy was deferred because of a previous splenectomy for purpura hemorrhagica. When the symptoms increased it was done, with considerable bleeding at operation but with a normal convalescence.

Recurrent or chronic appendicitis occurred in 38 cases. There was no operative mortality.

There were 33 cases of appendicitis with perforation, in 3 of which the patients died, a mortality of 9 per cent. As 1 was not operated on, the operative mortality was 6 per cent. In neither of the operative cases was death due to generalized peritonitis alone. One of these patients, a boy of five, died from acute edema of the lungs within twenty-four hours after operation. Only drainage of the appendiceal abscess had been done. This patient was given nitrous oxide, oxygen and ether anesthesia. Permission for autopsy was not obtained, so that the cause of the edema is unknown. The other patient died five days after operation from a complicating pneumonia; while no autopsy was performed, there was no abdominal distention, and the patient did not present the picture of terminal generalized peritonitis.

In 39 per cent of the perforating appendicitis cases the patients had taken cathartics. Eight had symptoms for twenty-four hours or less, the shortest time being eight hours. In 15 cases two days or less had elapsed between onset and admission; in 2 cases three days, in 3 four days, in 1 each six, seven and twelve days, and in 2 fourteen days.

In the 33 perforating cases there were 41 operations. In 1 case operation was not done because of poor general condition and peritonitis; a ruptured appendix and peritonitis were shown at autopsy. Drainage of an appendiceal abscess only was done in 4 cases, with 1 death. Appendectomy was done three or more months following drainage of an abscess in 3 cases. In 1 case an intussusception was found and reduced, but appendectomy was not done; later three recurrent appendiceal abscesses were opened before appendectomy could be performed, with final recovery. There was 1 case of pregnancy, with recovery and normal delivery at term following appendectomy and drainage.

Table 1 shows the types of appendicitis and of operation, with mortality statistics. Table 2 shows the postoperative complications in the different groups.

TABLE 1. *Types of Appendicitis and of Operation.*

	No. of Cases	Deaths No.	Deaths per cent
TYPE OF APPENDICITIS			
Acute	101	0	0
Chronic	38	0	0
Perforated	33	3	9
Totals	172	3	1.7
TYPE OF OPERATION			
Appendectomy	139	0	0
Appendectomy and drainage	26	1	4
Drainage of abscess only	4	1	25
None	2	1	50
Appendectomy after drainage of abscess	3	0	0
Exploratory laparotomy after drainage of abscess (appendix not found)	1	0	0

The early diagnosis and hospitalization of most of the 172 cases in this series is, we believe, a great credit to the physicians of our city and has been an important factor in the low mortality rate of 1.7 per cent. In the delayed cases the physician often had not been called until late. There were very few cases where delay in hospitalization had occurred because of difficulty in diagnosis. The practice of sending patients to the hospital for observation in

TABLE 2. *Postoperative Complications.*

Type of Appendicitis	No. of Cases	Incidence %	No. of Deaths
ACUTE APPENDICITIS			
Total complications	12	11	0
Wound sepsis	4	4	0
Hematoma wound	2	2	0
Postoperative hemorrhage of wound (re-operation)	1	1	0
Phlebitis of right leg	2	2	0
Massive collapse of lung	1	1	0
Bronchopneumonia	1	1	0
Enteritis	1	1	0
CHRONIC APPENDICITIS			
Total complications	4	11	0
Bronchopneumonia	1	3	0
Hematoma of wound	1	3	0
Stitch abscess	1	3	0
Hemorrhagic diathesis (transfusion)	1	3	0
ACUTE APPENDICITIS WITH PERFORATION			
Total complications	12	36	3
Pelvic abscess	5	15	0
Septic wound followed by hernia	3	9	0
Lobar pneumonia	1	3	1
Acute edema of lungs	1	3	1
No operation	1	3	1

all cases in which the presence of appendicitis is suspected is a good one, and should be observed more frequently. A campaign to acquaint the people of Fitchburg with the symptoms of appendicitis, and to impress on them the need for the immediate investigation of abdominal pain, the danger from the use of cathartics and, finally, the importance of time in the successful treatment of acute appendicitis, is urgently needed.

REFERENCE

1. Coller, F. A.; Dick, V. S., and Maddock, Walter G.: Maintenance of normal water exchange with intravenous fluids. *J. A. M. A.* 107:1522-1527, 1936.

REPORT ON MEDICAL PROGRESS

COMMUNICABLE DISEASES: CARDIOVASCULAR DISEASE IN DIPHTHERIA*

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THE lowering of the mortality of diphtheria through intubation and antitoxin has centered attention on the cardiovascular disorders of this disease. Malignant diphtheria continues to claim many lives in the early stage, owing to the fact that antitoxin is not given in the first hours. However, even in the recent epidemic years in Europe the malignant type constituted only about 10 per cent of all cases.[1] This type usually involves the fauces and posterior nasal vault, with a comparatively low incidence of laryngeal invasion.[2] Nevertheless, the clinician may be confronted by a condition that was for several days only a moderate diphtheria but that, through parental neglect, has assumed an advanced stage by the time of the physician's first visit. It is also possible for a slowly developing type suddenly to assume all the characteristics of a malignant infection. Consequently, from a clinical point of view, the term "malignant" may apply to any grave toxemia during the membranous stage.

EARLY CIRCULATORY FAILURE AND ITS TREATMENT

It is now generally conceded that early cardiovascular embarrassment is the result of toxemia, and as such differs from that seen in other acute infectious processes only in its possible malignancy and association with respiratory obstruction by the formation of membrane or by edema. It is well recognized that such obstruction is often above the glottis and can be effectively relieved by suction of this area. Too often restlessness, cough and cyanosis are ascribed to cardiac decompensation when actually a piece of freed membrane lodged in the glottis is responsible. Consequently, lowering the cough reflex with opiates is to be strictly avoided in the membranous stage.[3] This general intoxication, then, is the same as that seen in other septic conditions, unless respiratory obstruction creates a strain on the heart through violent respiratory efforts in the presence of anoxemia. There are fever and tachycardia. Difficulty or pain on swallowing often results in dehydration. The carbohydrate metabolism is disturbed in proportion to the toxemia. At first the glycogen is rapidly used up, giving rise to a decreased sugar content of the blood. If the toxemia is prolonged, this condition may change abruptly to an increased blood sugar, due in part to suppression of insulin but also to inability of the tissues to assimilate dextrose.[4] The blood pressure continues near normal[5]; the heart sounds are distinct and usually continue to be regular, unless death is imminent. Finally, there is anemia of the medullary centers.

Leete[6] has reviewed 4700 cases of faucial diphtheria which occurred during the recent epidemic in Hull, England. Among these there were 461 fatalities. In those patients who died early in the disease the general toxemia overshadowed any cardiac disturbance as a cause of death, an observation in accord with that of Gordon[3] at Detroit and my own in Boston.

The treatment here is not directed at the heart alone, because this organ is simply being poisoned along with other vital centers. Consequently, the best supportive measures consist of the vigorous administration of antitoxin, together with intravenous injections of 10 per cent dextrose — 100 to 500 cc. according to the age of the patient. The use of insulin in conjunction with dextrose has been shown to be ineffective by the controlled clinical observations of Begg.[7] In cases of very

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severe toxemia some physicians have given 30 cc. of 50 per cent dextrose in the first dose, using 1.0 unit of insulin intramuscularly with each gram of dextrose. At the Haynes Memorial Hospital we prefer the 10 per cent solution because dehydration is always present. A word of warning should be given in regard to the antitoxin. Of course, these severe cases need the maximum scale of dosage, and it is always desirable to introduce part of the antitoxin intravenously, but if circulatory collapse is already in progress great care must be taken not to cause a further drop in the blood pressure. Adrenalin must always be at hand. To offset circulatory collapse one may give the antitoxin either intravenously, diluted with 200 cc. of normal saline, or intramuscularly in the lateral aspect of the thigh, diluted with 100 cc. of normal saline. It should be administered very gradually, as is done in those individuals showing serum sensitivity to the preliminary skin test.

As for drugs, there is nothing to be said in their favor. Opiates, as has already been mentioned, are to be avoided in the membranous stage. The same applies to all sedatives. The natural state in this stage is one of apathy unless there is a mixed infection with a streptococcus. If, therefore, restlessness occurs it is likely to be the result of obstruction to breathing in one form or another. Suction, intubation or tracheotomy may be necessary, but the indications for these will be masked by opiates. Efforts directed at stimulating the circulation to the neglect of respiratory obstruction are poor medical practice. On the other hand, if no obstruction is present the profound toxemia causes death. Digitalis, as well as all the drugs of the digitalis group, is ineffective, if not actually harmful, owing to the possibility of the occurrence of beginning myocardial necrosis and inflammation. Furthermore, the heart poisoned by diphtheria is unusually susceptible to the action of digitalis,[8] and block may be induced. Camphor in oil, caffeine and Coramine have been found to be futile. The latest experimental and clinical studies[9–16] on the use of vitamins in diphtheria offer no encouragement.

Late Cardiovascular Disorders

A certain amount of confusion has crept into the literature in regard to the use of the term "late" as applied to cardiovascular disorders. In the first place, arbitrary periods in terms of the day of the disease are used to differentiate early and late. Secondly, the term "circulatory failure" has been used to embrace disorders which may or may not lead to true circulatory failure. Finally, too much effort has been expended in attempting to make a constant syndrome out of late circulatory failure when, as a matter of fact, it can be brought about through divergent pathologic processes that may operate either independently or in conjunction with each other.

Cardiac Involvement. In the malignant type of diphtheria, which overwhelms the patient from the beginning, evidence of myocarditis may appear as early as the third day. On the other hand, in the clinical type that has a more gradual or smoldering onset the signs may not appear until the fourth or fifth week. Furthermore, the promptness with which antitoxin is administered in either of these types may prevent, delay or modify the manifestations of cardiovascular damage.

Some confusion exists in the use of the term "malignant" because it has come to be applied in a bacteriological rather than a clinical sense. Thus, an epidemic in which the gravis strain predominates is described as an epidemic of malignant diphtheria even though only about 10 per cent of the total cases exhibit the fulminating type. Here we have mild cases designated as malignant because of the epidemiologic characteristics. The term "malignant" is used in the present paper in its clinical sense according to the well-known classifications of Marfan and Destéfano,[17] and not according to the presence of the gravis strain.

The term "late" as applied to cardiovascular disorders is employed here to denote that convalescence from the membranous stage is under way. The local lesion is undergoing repair or is entirely repaired, yet the bound toxin or its by-products in the tissues continue to influence the cardiovascular system. This can occur where a spontaneous recovery takes place without the administration of antitoxin. Myocarditis is the outstanding pathologic feature, and is present in most cases when circulatory failure occurs. The earlier the signs of myocarditis, the graver the prognosis. However, myocardial insufficiency is frequently only a contributory cause of death, in that paralysis of the vasomotor system is oftener the direct cause of the complete circulatory failure.

The earliest signs of myocarditis are found in the electrocardiogram.* In fact, it may show a high degree of heart block before this is suggested by clinical observations, and such observations clearly indicate impairment of the cardiac

*Observations on the oculocardiac reflex by Borgiotti[18] showed that electrocardiographic changes were induced which were not observed in the electrocardiogram taken before the test, suggesting that mechanical compression of the eyes brings out latent cardiac pathologic defects. Frontali[19] is of the opinion that this phenomenon is due to the effect of the diphtheria toxin on the nervous system and is therefore of extracardiac origin.

function.[20–22] It is in these cases that cardiac failure may come on with great rapidity and lead to the death of the patient. Natin and da Rin[17] in 1934 published a very extensive series of electrocardiographic records on 144 cases, embracing all the characteristic alterations found in diphtheria, with numerous modifications, and now serving as a standard reference work. Indeed, it is only by the electrocardiograph that one can properly determine the extent of the cardiac damage, knowledge so essential to the prognosis as well as to the duration of strict aftercare.

Symptoms and Signs. With this in mind, let us review as they appear the clinical symptoms, the electrocardiographic findings, the physiological and pathological situations which may confront us and the means which we have of dealing with them. The fact has already been stressed that the electrocardiograph picks up the first signs of damage to the myocardium, but of course the instrument is applied only from time to time. The clinician can usually determine the presence of cardiac injury without it, but he cannot thus determine the exact nature of the injury to the conduction system. This applies especially to auriculoventricular dissociation with ventricular tachycardia,[22] which frequently leads to a fatal termination. The first sound becomes soft, and is frequently replaced by a systolic murmur with a maximum intensity to the left of the sternum; or the first or second sound may be split. Cardiac dilatation can at times be quite obvious. Andersen[21] determined the existence of myocarditis clinically in 49 of 194 cases of severe diphtheria, in 60 of which the electrocardiograms showed evidence of the condition. Any irregularity of rhythm may take place, but the commonest change noted is a protodiastolic gallop. In certain cases this gallop varies greatly in its intensity.

In the convalescent stage, while the patient is often in a comfortable and cheerful state, he may suddenly develop epigastric pain, vomiting, pallor and a characteristic frightened look. The heart rate may be accelerated at first, and then become gradually slower and irregular, or it may continue to be rapid. The pulse is soft, and sweating may be pronounced. Sometimes the patient goes through several of these crises, in which the blood pressure may vary above and below normal. In such cases periods of ventricular fibrillation have preceded death.[17, 21] In fatal block the heart rate is likely to drop below 30, and with this there is sometimes precordial pain.

Electrocardiograms may show every variety of grave disturbance to the conduction system, both auriculoventricular and intraventricular (bundle-branch) block. Like gallop rhythm, the block may come and go, but its presence implies much greater danger than does the gallop. Place,[20] Alstead[23] and Burkhardt[22] are of the opinion that cases in which the electrocardiogram shows evidence of myocarditis without block invariably recover under proper treatment. Nathanson,[24] on the other hand, reported 2 sudden deaths in convalescents showing inverted T waves. Von Kiss,[25] from his large recent experience in Budapest, states that damage to the musculature as shown in pronounced changes in the T wave, with only slight or questionable involvement of the conduction system as shown by lowering of the QRS complex, may signify impending danger; further, that an inverted T wave in all three leads, or at least in Leads 1 and 2, means without doubt a severe myocardial lesion, with a probable fatal outcome. Alterations in the T wave are usually seen first in Lead 3, then in Lead 2 and finally in Lead 1. T-wave alterations — diphasic, isoelectric and inverted — are at times found in other infections, such as tonsillitis, scarlet fever, typhoid fever and pneumonia, but they are probably of graver significance in diphtheria. In diphtheria a combination of damage to the specialized conduction system and of injury to the myocardium in general is common. Conduction changes are more frequently observed in early childhood, while alterations in the T waves are more prevalent in older patients.[22] Bock[26] lays emphasis on a lengthened QT interval.

The advent of marked block usually precedes signs and symptoms of circulatory failure. Under these circumstances death may occur within a few hours, or be delayed for several days after increasing weakness. If myocardial insufficiency predominates, there are cardiac dilatation, cyanosis with mottling, sometimes cough and rales, extreme restlessness, epigastric pain, vomiting and enlargement of the liver. Myocardial insufficiency may occur without block, in which case there is increasing tachycardia. Heart block may appear and disappear several times during the day. This form of cardiac failure usually occurs in the first or second week of the disease.

Lesser disturbances of rhythm such as extrasystoles may be occasioned by irritation of the myocardium, but also by the action of the toxin on the parasympathetic nerves. This also applies in part to mild variations in the rate, in the form of relative tachycardia, bradycardia and cardiac irritability.[27] A lowering of the tone of the sympathetic control is sometimes accompanied by marked lowering of the white-cell count, with a relative lymphocytosis. In fact, these findings

have served as a warning of impending vasomotor collapse.[2]

Peripheral Circulatory Failure. While myocarditis of some degree is almost invariably found at autopsy in late circulatory failure, it is, as we have already remarked, oftener only a contributory cause of death, the commonest cause being vasomotor paralysis. This paralysis is not of central origin but is in the myoneural junction or motor end plates of the parasympathetic nerves of the splanchnic vessels, being a manifestation of the polyneuritis that constitutes postdiphtheritic paralysis. Thus, it coincides with the onset of other paralyses such as the palatal and oculomotor. Furthermore, it is not to be confused with respiratory paralysis involving the phrenic and intercostal nerves, in which the respirator may be the means of saving the patient's life.

Vasomotor paralysis is in itself the commonest vascular syndrome complicating diphtheria, and this extracardiac condition, even in the presence of advanced myocardial damage, tends to overshadow disorders arising within the heart. The syndrome consists of marked pallor, in which the patient takes on a gray color or that resembling alabaster, along with a peculiar frightened look in children. The skin becomes cold. There is epigastric pain with vomiting. Without block the heart tends to become rapid as the blood settles in the relaxed and engorged splanchnic vessels. The volume of blood in the heart is diminished, and the blood pressure falls. With well-marked heart block, the chambers have time to fill and the pulse can be obtained; otherwise it is likely to be lost. In a few hours the patient may be dead, or this condition may continue for several days and then lead to a sudden fatal termination or to recovery.

Intracardiac Thrombosis. One type of myocarditis which occasionally occurs in the very toxic form of diphtheria is that associated with the formation of a thrombus, a condition resulting from extensive inflammation or hemorrhage within the myocardium and the overlying endocardium in conjunction with dilatation. Of course, the pathologic state of severe diphtheria, like that of severe scarlet fever, includes a hemorrhagic tendency, and it is not surprising that this should appear in the heart itself. I have seen a large, pendulous thrombus originating in the left auricle, reaching well into the mitral orifice and before death giving rise to an indescribable clatter of heart sounds. Chiari[28] describes one of these cases which at autopsy showed marked fatty degeneration and a thromboendocarditis, from which diphtheria bacilli were recovered in pure culture. In a later communication[29] he reports the autopsy of a ten-year-old girl who with extensive membrane died suddenly on the fifth day from "heart collapse," without any previous signs of cardiac disorder having been noticed. The heart showed marked fatty degeneration, with many hemorrhages under the epicardium, in the myocardium and under the endocardium. These were particularly marked in the right auricle in the region of the sinus and the atrioventricular node. There was marked cardiac dilatation, especially on the right, and the mitral valve showed a fibrinous exudate from which was obtained a pure culture of diphtheria bacilli. Harding[30] reports no less than eight attached blood clots found within heart chambers at autopsy. Such thrombi may be the source of emboli that are carried to various organs, giving rise to repeated infarctions in the brain or lungs, with sudden hemiplegia and pulmonary signs.[2] According to Rolleston,[31] hemiplegia, in contrast to other palsies arising from diphtheria, has its origin primarily in damage to the blood supply by embolism, thrombosis or hemorrhagic encephalitis, of which embolism is the commonest. The difficulties in diagnosing cerebral emboli are discussed by Zischinsky[32] in a review of 14 cases from his Vienna clinic.

Endocarditis. Vegetative endocarditis of the mitral valve from which the diphtheria bacillus was recovered in pure culture has been reported.[33–35] It is true that in 1 of these cases[33] a previous rheumatic endocarditis existed prior to the onset of diphtheria. But it is significant that the diphtheria bacillus set up a local process in this already damaged valve, causing death. A true vegetative endocarditis in the course of diphtheria is an extremely rare phenomenon; therefore, the heart murmurs usually heard are not due to valvular endocarditis.

Postdiphtheritic Neurocirculatory Asthenia. A mild but disturbing cardiovascular disorder may occur in the late convalescence of some cases of diphtheria. I refer to a curious irritability of the pacemaker which often results in an evening tachycardia persisting for three to eight weeks. This can happen when vascular collapse has not taken place and when the myocardium has escaped injury. It may also take the form of a persistent relative tachycardia or bradycardia or an "effort syndrome," being similar to the condition sometimes following other infections such as typhoid fever and influenza. It may have its origin within or outside of the heart, that is, in the sinus node or in the parasympathetic vagus nerves.

Pathologic Changes

The pathologic changes found in early circulatory failure in diphtheria are due to an overwhelming toxemia, and sometimes include dilatation of the heart. Masshoff,[36] in a postmortem study of 20 hearts, found that dilatation of the auricles was greater than that of the ventricles, and that the bicuspid valve was most frequently dilated, the right side of the heart being more involved than the left, as shown by microscopic sections. However, such changes are by no means constant, and one may often search in vain at autopsy for evidence of injury in the heart or anywhere in the nervous system as even a contributory cause of death.[25] In a more prolonged toxemia the myocardium may begin to show parenchymatous hyaline degeneration or necrosis. The longer the myocarditis lasts before death occurs, the more pronounced and extensive this change becomes.[25] The toxin seems to show no partiality for either the conduction system or the contractile tissues. Friedemann[37] is of the opinion that the toxin of diphtheria injures the walls of the coronary vessels, and that in time this brings about disturbances in the conduction system, thus explaining the latent period. The evidence of true myocarditis consists of necrosis and the inflammatory process of repair. Complete regeneration or fibrosis may follow. Sometimes the inflammatory infiltration as part of the process of repair appears to choke the nutrition of the healthier muscle fibers.[38] Occasionally the heart appears normal until careful search shows a small inflammatory area about the bundle. Deaths in these cases were formerly attributed to vagus degeneration. At other times, the extent of myocardial damage found at autopsy is astonishing. Occasionally such large patches of fatty degeneration are observed that it makes one wonder how the heart could have continued beating so long.

Duration of Cardiac Damage

Findings at routine postmortem examinations strongly suggest that some individuals long since recovered from diphtheria may carry permanent scars through life in the form of areas of fibrosis in the myocardium.[39] However, this can be taken only as presumptive evidence of permanent damage from diphtheria. The temptation of many observers has been to correlate these late findings with the large areas of fatty degeneration mentioned above. I once held the view that permanent cardiac damage was to be expected. Recent evidence on the duration of myocardial damage after diphtheria has caused me to alter my opinion.

In 1905, F. W. White[40] reported on 78 cases examined by him six to twelve months after they had exhibited heart complications during diphtheria. He pointed out that a return to normal in some severe cases required weeks or even months. Many subsequent observers have determined that recovery promises complete regeneration of the heart muscle so that eventually the electrocardiogram becomes entirely normal, even though the heart may continue to show the effects of injury for months. Mautner[41] reports a typical example, in which block persisted for eighteen months. Von Kiss[42] reports a case in which heart damage persisted for five years after diphtheria, and another in which bundle-branch block with myocardial insufficiency persisted for ten years.

Andersen[21] examined 24 patients eight years after recovery from diphtheria, none of whom had had any infection in the intervening period that would suggest myocardial involvement. Among 15 with definite electrocardiographic changes during diphtheria, 7 continued to show these changes. Among 12 who showed clinical signs of myocarditis during the attack, 4 continued to show signs of myocardial insufficiency. In all, 16 patients showed abnormal electrocardiograms. Andersen supports his observations by referring to Schwensen,[43] who in 1922 drew the conclusion that diphtheria must be considered an important cause of heart failure in later life. The criteria on which he bases this statement cannot be considered as first-rate evidence, and he admits that in some of the cases studied only doubtful signs of myocarditis existed at the time of their stay in the hospital with diphtheria.

Alstead[23] studied 150 patients who were known to have had severe diphtheria; in 90 of these he found a negative or isoelectric T wave in Lead 3, whereas this was found in only 30 of his 100 controls. He acknowledged that this finding could not be accepted as evidence of myocardial disease and pointed out that regardless of whatever its significance might be there was certainly no coexistent clinical abnormality.

Jones and P. D. White[44] in 1927 studied 100 patients who had suffered from severe diphtheria five to ten years previously at the Boston City Hospital, 12 of whom were originally diagnosed as having had myocarditis. Clinical, radiographic and electrocardiographic examinations failed to reveal any appreciable chronic effect of the disease on the heart. Ninety-one of these patients were re-examined after another ten years by Thompson, Golden and P. D. White,[45] and 9 more were added from the original period to make up an even 100. In none of these was there any

positive proof of abnormalities resulting from the diphtheria, nor had evidence of any cardiac disturbance resulting from it made an appearance within the interval of fifteen to twenty years. These cases are to be studied again in 1947.

The term "myocarditis" is often used loosely to denote circulatory failure. A relatively mild myocarditis associated with vasomotor collapse would not be expected to give rise to as lasting myocardial damage as a more severe myocarditis in which vasomotor collapse was averted. There must always be an element of doubt regarding the diphtheritic origin of heart disease developing in later years where no myocarditis existed during or immediately after the diphtheria. Therefore, with due consideration of our knowledge of the pathology and the process of repair, particular interest centers in the subsequent history of those cases exhibiting indisputable signs of severe myocardial injury as a result of diphtheria.

In 70 cases of severe diphtheritic myocarditis treated at the *Plauen Stadtkrankenhaus,* Behr[46] continued the electrocardiographic examinations in the survivors for a period of two years. He found that damage to the musculature of the auricle, as suggested by abnormalities in the P wave, was restored more quickly than was damage to the ventricle. Patients with a continued complete block and slow ventricular rhythm invariably died, while those in which the complete dissociation lasted only a minute or two often recovered. During the shift from partial to complete block with a long ventricular pause the Morgagni-Adams-Stokes syndrome developed. One block continued in evidence for months but cleared up entirely in two years. Bundle-branch block, with its sudden and so often fatal outcome, was usually slow in clearing up, but even here the survivors eventually showed a complete return to normal. Changes in the T wave during the acute disease usually appeared first in Lead 3 and then in Leads 2 and 1. But in this event, if the patient survived the early period, there was a tendency for the T waves to revert to normal in the course of days or weeks. At the follow-up electrocardiographic examinations one and two years later there was nothing to suggest organic or functional heart disease. It is to be hoped that these cases, so carefully followed from the start, will be followed up in the same manner that is being carried out by Dr. Paul D. White and his associates.

It is always difficult to prove that a myocardial failure developing in later life is related to a severe diphtheria of childhood.[45, 47] Circumstantial evidence is supplied by Butler and Levine[48] in a group of 20 patients having proved heart block without the usual causes, such as arteriosclerosis, syphilis, coronary disease, digitalis, fever and rheumatic infection. However, congenital block could not be ruled out in this small group. Fifty per cent of the patients had a history of diphtheria in childhood, as compared to 6 per cent in 600 consecutive control surgical cases. The average age of the patients who had had diphtheria was eleven years lower, and their average systolic blood pressure was 40 mm. lower, than in those who had not. Reid[49] cites a girl of ten who showed a permanent bradycardia, presumably dating back to a severe attack of diphtheria five years previously. She was leading a normal life. Faulkner[50] reports 2 cases with permanent abnormalities dating back to diphtheria; one patient was a machinist leading a normal life with a high take-off of T_2 and a prolonged PR interval, and the other a woman leading an active life who had passed through an uneventful pregnancy with a complete heart block.

With the evidence at hand one is forced to conclude that if the heart has shown no signs of impairment within six weeks of the attack of diphtheria, there is as yet no definite proof that it will be more prone to heart disease in later life. Furthermore, when injury to the muscular or conduction system fails to cause death at the time of the myocarditis, the tendency is toward complete recovery. The muscular system generally returns to normal more promptly than does the conduction system, bundle-branch block being the slowest to recover. True myocarditis of diphtheria is an inflammatory response to degeneration, and as such is a process which tends either to kill or to permit a return to normal. Rare cases of permanent block are on record, but most of these are not attended with myocardial insufficiency. Whether a persistent, purely functional defect leads to impairment later in life is as yet unknown. Well-controlled investigations are under way, and one awaits with great interest the reports from carefully followed cases as the patients pass the age of fifty.

Incidence of Severe Circulatory Disturbance

The incidence of myocarditis in diphtheria can be seen in Table 1, comprising 15,490 cases compiled from hospital records in three American cities. The term "myocarditis" as used here is based largely on the clinical diagnosis, with an indefinite amount of support from electrocardiograms and autopsies, which after all constitute the final criteria for this diagnosis. Hoyne and

Welford[51] found that the mortality rate in cases showing myocarditis was 75 per cent in patients under five years of age, 54 per cent in those from six to ten, 50 per cent in those from eleven to fifteen and 43 per cent in those over fifteen. As regards the relation of the type of diphtheria to the death rate, it was found that in the simple tonsillar form the mortality rate was only 11 per cent, as compared with 54 per cent when the membrane had spread to the uvula and pharynx and 70 per cent when it had spread also to the nose.

Thoenes[52] analyzed 1124 cases of diphtheria at Cologne during 1929–1930. One hundred and eighty-six patients (16.5 per cent) showed severe circulatory disturbance, and 54 of these (29 per cent) died. The original infection in the fatal cases was severe in 47, moderately severe in 4 and apparently mild in 3. Death occurred in 11 cases between the second and seventh days, in 33 cases between the eighth and fourteenth days and in 9 cases between the fifteenth and twenty-third days. One patient died on the forty-second day. Thoenes's classification of early and late failure differs from mine in that the late form includes only those arising at the time of postdiphtheritic paralyses, a method of grouping used in various European clinics.

Behr[46] in Plauen, studied 230 patients with malignant diphtheria, of whom 84 (36 per cent) died. His electrocardiographic findings and follow-up results have been mentioned above. Among 70 children, myocardial changes appeared in the first week in 28 cases, and of these patients 24 died of heart failure, 2 died of respiratory paralysis and 2 survived. In the course of the second week 35 patients developed myocarditis, 2 of whom died of heart failure, 1 died of respiratory paralysis and 32 lived. During the third week 7 patients developed myocarditis, and only 1 of these died. Thus we see that the earlier the signs of myocarditis appear, the more serious is the prognosis.

The routine use of the electrocardiograph on diphtheria wards is sure to give a much greater recognition of myocarditis than has hitherto been obtained by routine clinical examinations and electrocardiograms of severe cases only. Anderson[21] selected 194 moderate and severe cases for electrocardiographic study. He found that only 24 per cent of those with moderate diphtheria and 11 per cent of those with the severe type failed to show evidence of myocarditis. This study was made in 1933 in Copenhagen, where malignant diphtheria was prevalent and where the incidence of myocarditis would consequently be high.

In an extensive study of 144 cases of diphtheria in Buenos Aires, Natin and da Rin[17] found electrocardiographic alterations in 62 cases, as shown in Table 2. On the other hand, in New York City recent serial electrocardiograms of 140 patients showing toxic diphtheria manifested alterations in only 28.[22] It is difficult to attribute these wide variations in electrocardiographic findings entirely to the relative prevalence of malignant diphtheria in these different parts of the world. Obviously this clinical type gives rise to a greater incidence of myocarditis, but it is equally obvious that the electrocardiographic interpretations made by Burkhardt and his associates in New York City are more

TABLE 1. *Incidence of Clinical Myocarditis and Mortality in Diphtheria in Three American Hospitals.*

AUTHOR	HOSPITAL AND LOCALITY	NO. OF CASES OF DIPHTHERIA	NO. OF DEATHS FROM DIPHTHERIA	MORTALITY	NO. OF DEATHS WITH MYOCARDITIS AS A CONTRIBUTORY CAUSE	MYOCARDITIS MORTALITY IN RELATION TO TOTAL DEATHS
				%		%
Hoyne[51]	Metropolitan, Chicago	4671	548	11.6	308	56.2
Gordon[3]	Herman Kiefer, Detroit	4751	599	12.6	375	62.6
Wesselhoeft	Haynes Memorial, Boston	6068	602	9.9	356	59.1
Totals		15490	1749		1039	
Averages				11.3		59.4

In these three series, myocarditis as a cause of death is very much the same, as seen by the figures in the last column. In the recent European epidemics of malignant diphtheria, myocarditis and acute toxemia became a more frequent cause of death, while laryngeal diphtheria diminished in this respect.

TABLE 2. *Electrocardiographic Alterations in Relation to Type of Diphtheria (Natin and da Rin[17]).*

TYPE OF DIPHTHERIA	ELECTROCARDIOGRAPHIC ALTERATIONS
	%
Mild tonsillar (without edema)	7.6
Severe tonsillar (with edema)	15.0
Submalignant unilateral, faucial	25.0
Submalignant bilateral, faucial	42.0
Malignant, slow	79.4
Malignant, rapid and hemorrhagic	100.0

conservative than those of Andersen at Copenhagen. A greater uniformity in these interpretations is therefore desirable in establishing the incidence of myocardial damage, which plays such an important part in the severe circulatory disturbances of diphtheria.

The number of possible combinations of functional disease makes it impossible to lay the blame for late circulatory failure on any one factor, or to expect any uniformity in the clinical picture. Furthermore, these disturbances frequently arise so late — and as part of the postdiphtheritic polyneuritis — that their clinical counterpart is inapplicable to those animal experiments dealing at most with a merging of the toxemic stage with myocardial injury. Indeed, I am reminded of the statement of Friedberger[53] that natural diphtheria in man is as different from the toxin-produced diphtheria in the guinea pig as a man is from a guinea pig. This applies equally well to experimental circulatory failure in animals and the late circulatory failure observed in man. Such a clinical point of view in no way belittles the work of Enriquez,[54] Romberg,[55] Porter,[56] Yabe[57] and Edmunds[58, 59] and others, any more than it belittles the mass of invaluable data afforded by animal experimentation in the entire field of diphtheria. It merely draws attention to the limitations of their clinical applicability.

Treatment of Late Circulatory Disorders

In the treatment of late circulatory failure in diphtheria there are many possibilities to be considered, and therefore no hard and fast rules of management can be laid down. Actually, in every case it must be decided whether failure exists or is threatening. The mere presence of dysfunction as manifested by gallop rhythm or mild conduction disturbances demands no more than complete rest in bed. On the other hand, any moderate amount of diphtheritic membrane in the initial stage is a potential source of late cardiovascular disorder, and any severe formation of membrane requires prolonged bedrest, preferably with hospital facilities. Early and adequate treatment in the acute stage will do much to prevent late circulatory failure.

Once the seriousness of the situation is established through signs and symptoms, any one of the combinations of cardiac abnormalities is a possibility, with or without disturbed peripheral circulation, splanchnic congestion and oligemia. As regards the myocardial condition, the question arises as to whether digitalis is indicated. The functional disturbance here can be so similar to that observed in acute digitalis poisoning that one would hesitate to consider any dosage that would fulfill the term of "digitalization," since further blocking is to be feared. If small doses are to be used, how small must these be in order to avoid danger? The answer of most clinicians is to advise against employing it at all, with which I am in agreement, in spite of evidence that this drug is capable of exerting its beneficial influence on the undamaged areas of the heart. The reason for this stand is that although the drug might be helpful on one day, the situation might be so altered on the next as to contraindicate it without means of counteracting its influence. Such competent clinicians as von Bokay[2] and his successor, von Kiss,[60] in Budapest, have given small daily doses with careful electrocardiographic controls in the earliest stage of myocardial dysfunction, but any attendant improvement in the metabolism of the heart muscle which they ascribed to it was probably due to the dextrose administered intravenously in combination with this drug. Digitalis is therefore contraindicated, and this applies to all other drugs of the digitalis group. However, in the later weeks of convalescence, if signs of decompensation appear, digitalis should be tried cautiously. There is no advantage in using the less standardized drugs of the group, such as ouabain and strophanthus. Alcohol, caffein, camphor, strychnine and Coramine continue to have their advocates, but in my hands they have proved valueless.

I now come to a consideration of the disturbed peripheral circulation due to vasomotor paralysis with relaxed splanchnic vessels and oligemia. This syndrome appears rather abruptly. There is logic in the assumption that adrenalin might be helpful, but the condition is always too far advanced to yield to this drug. Then again, there is logic in the use of Pitressin (beta hypophamine) with low blood pressure. It has a longer and more powerful action than has adrenalin. Gordon[3] has found it of value in subcutaneous doses of 0.25 to 1.00 cc. at eight-hour to twelve-hour intervals, being guided by blood-pressure readings. These doses must always be preceded by the giving of fluids or, in the event of vomiting, by intravenous injections. He used 10 per cent dextrose — 100 cc. for an infant, 500 cc. for a child, 1000 cc. for an adult each day. Schwentker and Noel[61] see no justification for forcing fluids in this later circulatory collapse, but they do not consider the simultaneous use of Pitressin. My experience at the Haynes Memorial Hospital has not suggested that intravenous dextrose alone is of any appreciable value in late vasomotor paralysis. Furthermore, it is worthy of mention that one may encounter great difficulty in getting the

needle into a collapsed vein, especially in the case of a small child. Dieckhoff[14] found that Veritol (Paredrinol*) raised the blood pressure in late vascular collapse both in animal experimentation and at the bedside. There were 4 deaths among his cases attributable to myocarditis, which was established by the electrocardiograph.

During the last twenty-five years a number of other measures have been advocated for this condition. Among these, the use of an abdominal binder and the raising of the foot of the bed, as recommended by Harding,[30] seemed particularly hopeful. At the Haynes Memorial Hospital raising the foot of the bed never appeared to accomplish anything. On the contrary, children would exhaust their waning strength to get into a more comfortable position. The binder still meets with favor. Another simple measure which at times seems at least temporarily helpful is to supply warmth in cases where the color becomes alabaster and the skin cold. This can be done with hot-water bottles or a wire-covered electric-light bulb. In some cases a pink color actually returns. Friedemann[27] used baths, working the temperature up from 35 to 39°C. (97 to 104°F.). I have tried vigorous friction many times, but never with success. Of all the many measures employed in various parts of the world to combat circulatory collapse, the only one that has consistently reduced the mortality in hospitals is the vigorous intravenous administration of dextrose in all advanced cases of diphtheria. As with antitoxin, the beneficial action of this substance is essentially protective.

How long after recovery from circulatory disorders should a patient be kept in bed? The answer depends on the severity of the disorder and the duration of signs and symptoms; generally speaking, the patient should remain in bed until the electrocardiogram has become normal.[62] Roughly, all patients with severe diphtheria with evidence of myocarditis should be kept in bed for six to eight weeks, and those without electrocardiographic control or clinical signs of myocarditis for four or five weeks. Patients on my service showing a postdiphtheritic neurocirculatory asthenia, in the absence of any evidence of myocardial damage, are generally kept in bed four weeks. After this they are allowed out of bed, with their activities restricted according to the behavior of the heart. Medication is quite unnecessary. Adults should have the condition carefully explained in order to gain their confidence and co-operation.

In conclusion, I believe that late circulatory failure presents such a complication of possibilities that every effort should be made to determine the predominating factors and to try to correct these with the most direct and simple measures. A prolonged rest in bed of at least six to eight weeks is the proper safeguard during the repair of severe cases. It is needless to say that the proper facilities for the care of cardiovascular disorders in the course of diphtheria exist only in a hospital equipped for the purpose.

*Paredrinol is Smith, Kline and French's trade name for racemic para-hydroxy-a,N-dimethyl-phenethylamine, referred to abroad under the name Veritol (Knoll H-75).

The author expresses his indebtedness to Dr. Paul D. White for much valuable criticism of the manuscript and for the clarification of many uncertainties in the field of cardiology which beset one who deals with the problems of acute infections.

References

1. Hottinger, A., and Toepfer, D.: Ueber den Wert der Serumtherapie bei Diphtherie insbesondere bei der malignen, toxischen Form. *Ztschr. f. Kinderh.* **54:**505-529, 1933.
2. v. Bokay, J.: Die Diphtherie seit Bretonneau. *Ergebn. d. inn. Med. u. Kinderh.* **42:**463-634, 1932.
3. Gordon, J. E.: unpublished data.
4. Schwentker, F. F., and Noel, W. W.: The circulatory failure of diphtheria. *Bull. Johns Hopkins Hosp.* **45:**276-294, 1929, and **46:**259-271, 1930.
5. v. Kiss, P.: Ueber diphtheritische Herzstörungen. *Ztschr. f. Kreislaufforsch.* **28:**753-759, 1936.
6. Leete, H. M.: The heart in diphtheria. *Lancet* **1:**136-139, 1938.
7. Begg, N. D., and Harries, E. H. R.: Toxic diphtheria: the significance of sugar-tolerance curves and the value of insulin. *Lancet* **1:**480-485, 1935.
8. Edmunds, C. W.: Circulatory collapse in diphtheria. *Am. J. Dis. Child.* **54:**1066-1079, 1937.
9. Pakter, J., and Schick, B.: Influence of vitamin C on diphtheria toxin. *Am. J. Dis. Child.* **55:**12-26, 1938.
10. Peters, B. A., and Cunningham, R. N.: Vitamin B_1 and diphtheria. *Lancet* **1:**563, 1937.
11. Zilva, S. S.: The alleged antitoxic action of vitamin C in diphtheria. *Brit. J. Exper. Path.* **18:**449-454, 1937.
12. Schumann, H.: Ueber den Kohlehydratstoffwechsel des Herzmuskels diphtheriekranker und diphtherietoxinvergifteter Tiere. *Ztschr. f. d. ges. exper. Med.* **105:**14-22, 1939.
13. Dieckhoff, J., and Schüler, K.: Zur Behandlung der toxischen Diphtherie mit C-Vitamin und Nebennierenrindenhormon. *Klin. Wchnschr.* **17:**936-938, 1938.
14. Dieckhoff, J.: Kreislauf bei toxischer Diphtherie bzw. experimenteller Diphtherieintoxikation und seine Beeinflussung durch Veritol. *Klin. Wchnschr.* **16:**1154-1157, 1937.
15. Gukelberger, M., and Kahn, H.: Die Wirkung des Vitamins C auf die labile Gewebsoxydase des Herzmuskels im Verlauf der experimentellen Myocarditis diphtherica. *Ztschr. f. d. ges. exper. Med.* **103:**343-349, 1938.
16. Werner, S.: Zur Therapie der malignen Diphtherie mit Vitamin C und Nebennierenrindenextrakt. *Klin. Wchnschr.* **17:**17-20, 1938.
17. Natin, I., and da Rin, C.: Alteraciones electrocardiográficas en la difteria. Su relación con la miocarditis, el sindrome de Marfan, las causas de muerte y la muerte brusca. *Semana méd.* **1:**1789-1861, 1934.
18. Borgiotti, G. C.: L'indagine elettrocardiografica del riflesso oculo cardiaco nel difterico e nel non difterico ed il suo valore semeiologico esponente dello stato del miocardio nella difterite. *Riv. di clin. pediat.* **35:**886-911, 1937.
19. Frontali, G.: Squilibrio neuro-vegetativo e miocardite nell'intossicazione difterica. *Riv. di clin. pediat.* **36:**385-396, 1938.
20. Place, E. H.: Heart in diphtheria and scarlet fever. *New Eng. J. Med.* **207:**864-874, 1932.
21. Andersen, M. S.: Electrocardiographic studies on diphtheric myocarditis. *Acta med. Scandinav.* **84:**253-312, 1934.
22. Burkhardt, E. A.; Eggleston, C., and Smith, L. W.: Electrocardiographic changes and peripheral nerve palsies in toxic diphtheria. *Am. J. M. Sc.* **195:**301-313, 1938.
23. Alstead, S.: The heart after diphtheria. *Lancet* **1:**413-415, 1933.
24. Nathanson, M. H.: The electrocardiogram in diphtheria. *Arch. Int. Med.* **42:**23-46, 1928.
25. v. Kiss, P.: Ueber die Herzstörungen während und nach der Diphtherie. *Acta paediat.* **16:**414-423, 1933.
26. Bock, H.: Untersuchungen über die QT-Distanz im Elektrokardiogramm bei Diphtherie des Kindes. *Ztschr. f. Kreislaufforsch.* **30:**761-769, 1938.
27. Seckel, H.: Herz- und Kreislaufreflexe bei kindlicher Diphtherie. *Jahrb. f. Kinderh.* **143:**269-305, 1934.
28. Chiari, H.: Zur Frage der Diphtherie-Endokarditis. *Centralbl. f. allg. Path. u. path. Anat.* **58:**193-198, 1933.
29. *Idem:* Zur Frage des Uebertretens der Diphtheriebazillen in die Blutbahn und ihrer Ansiedlung in inneren Organen. *Wien. klin. Wchnschr.* **48:**685, 1935.
30. Harding, M. E.: *The Circulatory Failure of Diphtheria.* 176 pp. London: University of London Press, 1920. Pp. 84, 142.

31. Rolleston, J. D.: *Acute Infectious Diseases.* 376 pp. New York: Physicians and Surgeons Book Co., 1925. P. 28.
32. Zischinsky, H.: Embolie im Rahmen der diphtherischen Kreislaufstörung. *München. med. Wchnschr.* **85:**1221-1224, 1938.
33. Buddingh, G. J., and Anderson, K.: Acute vegetative endocarditis caused by *Bacillus diphtheriae. Arch. Int. Med.* **59:**597-601, 1937.
34. Kaschel, H.: Beitrag zur Diphtheriebacillensepsis. *Zischr. f. Kinderh.* **59:**437-445, 1938.
35. Lenti, P., and Wirz, S.: Étude clinique anatomo-pathologique et bactériologique d'une septicémie à bacilles diphthériques avec endocardite, apparue au cours d'une angine diphthérique. *Ann. de méd.* **44:**293-312, 1938.
36. Masshoff, W.: Untersuchungen über den Einfluss der Diphtherie auf die Grössenverhältnisse des Herzens und auf die geweblichen Veränderungen am Herzmuskel. *Arch. f. Kreislaufforsch.* **3:**142-167, 1938.
37. Friedemann, U.: Pathogenese der diphtherischen Kreislaufschwäche. *Deutsche med. Wchnschr.* **58:**1683-1686, 1932.
38. Warthin, A. S.: Myocardial lesions of diphtheria. *J. Infect. Dis.* **35:**32-66, 1924.
39. Schuppler, H.: Zur Frage der dauernden Herzschädigung nach Diphtherie. *Jahrb. f. Kinderh.* **145:**135-139, 1935.
40. White, F. W.: The after-effects of diphtheria on the heart. *J. A. M. A.* **45:**1243-1248, 1905.
41. Mautner, H.: Bleibende Herzschädigung und Reizleitungsstörung nach Diphtherie. *Med. Klin.* **30:**669, 1934.
42. v. Kiss, P.: Dauernder Herzblock nach Diphtherie. *Jahrb. f. Kinderh.* **151:**347-350, 1938.
43. Schwensen, C.: Heart rhythm in diphtheria. *J. Infect. Dis.* **30:**279-298, 1922.
44. Jones, T. D., and White, P. D.: The heart after severe diphtheria. *Am. Heart J.* **3:**190-195, 1927.
45. Thompson, W. P.; Golden, S. E., and White, P. D.: The heart fifteen to twenty years after severe diphtheria. *Am. Heart J.* **13:**534-541, 1937.
46. Behr, W.: Ueber zeitlichen Beginn und Dauer des diphtherischen Herzschadens. *Zischr. f. Kreislaufforsch.* **27:**793-804, 1935.
47. Beer, A.: Zur Frage der Dauerschädigung des kindlichen Herzens nach Diphtherie. *Jahrb. f. Kinderh.* **148:**152-169, 1936.
48. Butler, S., and Levine, S. A.: Diphtheria as a cause of late heart-block. *Am. Heart J.* **5:**592-598, 1930.
49. Reid, W. D.: Permanent bradycardia following diphtheria: case report. *Am. Heart J.* **5:**524-527, 1930.
50. Faulkner, J. M.: Electrocardiographic observations in diphtheria. *M. Clin. North America* **16:**993-1001, 1933.
51. Hoyne, A. L., and Welford, N. T.: Diphtheritic myocarditis: review of four hundred and ninety-six cases. *J. Pediat.* **5:**642-653, 1934.
52. Thoenes, F.: Die Prognose der diphthero-toxischen Herz- und Kreislaufstörungen im Kindesalter. *Monatschr. f. Kinderh.* **53:**381-389, 1932.
53. Friedberger, E.: Hat das normale Pferdeserum einem Einfluss auf die experimentelle Infektion des Meerschweinchens mit diphtheriebazillen? *Klin. Wchnschr.* **56:**151-158, 1919.
54. Enriquez and Hallion: Recherches expérimentales sur la toxine diphthérique: ses effets sur la circulation et la respiration. *Arch. de physiol. et de path. gen.* Series 5, **10:**393-408, 1898.
55. Romberg, E.; Pässler, H.; Bruhns, C., and Müller, W.: Untersuchen über die allgemeine Pathologie und Therapie der Kreislaufstörung bei acuten Infectionskrankheiten. *Deutsches Arch. f. klin. Med.* **64:**652-714, 1899.
56. Porter, W. T., and Pratt, J. H.: The state of the vasomotor centre in diphtheria intoxication. *Am. J. Physiol.* **33:**431-440, 1914.
57. Yabe, S.: The action of diphtheria toxin upon the circulation. *J. Pharmacol. & Exper. Therap.* **19:**1-11, 1922.
58. Edmunds, C. W., and Cooper, R. G.: Action of cardiac stimulants in circulatory failure due to diphtheria. *J. A. M. A.* **85:**1798-1801, 1925.
59. Edmunds, C. W., and Johnston, F. D.: The circulatory collapse in diphtheria. *J. A. M. A.* **90:**441-444, 1928.
60. v. Kiss, P.: Wann soll bei Diphtherie Digitalis gegeben werden? *Klin. Wchnschr.* **13:**411-413, 1934.
61. Schwentker, F. F., and Noel, W. W.: The circulatory failure of diphtheria. *Bull. Johns Hopkins Hosp.* **46:**359-364, 1930.
62. v. Kiss, P.: Wie lange bedürfen Diphtheriekranke der Bettruhe? *Monatschr. f. Kinderh.* **60:**426-435, 1934.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

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CASE 26281

PRESENTATION OF CASE

First Admission. A twenty-two-year-old single girl student was admitted to the hospital complaining of weakness.

The patient was in fairly good health until two years before admission, when she began to tire easily and complain of insomnia and weakness which steadily progressed. She had had amenorrhea for five years, and before this time the menses had been irregular and scanty. Approximately six months before admission she was treated for two months with liver extract for anemia, which was thought to have possibly resulted from frequent epistaxes which she had experienced all her life; on occasions she bled as much as 2 ounces or more. About one month after liver therapy was stopped, she noticed a general bronzing or yellowing of the skin; the scleras were not jaundiced. No change in the color of the urine or clay-colored stools appeared. There were no puritus, abdominal symptoms, indigestion weight loss, dyspnea, palpitation, cough, hemoptysis or night sweats. One week before entry, when seen by a physician, bile was discovered in the urine.

The family and past histories were noncontributory.

Physical examination revealed a fairly well-developed and well-nourished woman in no apparent distress. The skin was evenly brown, without splotching, or increased pigmentation in the axillas; it was greasy, with an acneform eruption over the face and chest. There was hypertrichosis of the arms, face and abdomen, with masculine distribution of the pubic hair. The head hair was stiff and dry. The mucous membranes were pale, with no abnormal pigmentation. The scleras were slightly jaundiced. The heart, lungs, abdomen and remainder of the examination were negative.

The temperature, pulse and respirations were normal.

Examination of the blood showed a red-cell count of 3,400,000 with 70 per cent hemoglobin, a white-cell count of 4000 with 67 per cent polymorphonuclears, a normal smear, and a reticulocyte count of 1.9 per cent. The urine and stools were essentially negative; one specimen of urine gave a + test for bile. A blood Hinton test was negative. The icteric index was 35 per cent; the van den Bergh 6.8 mg. bilirubin per 100 cc., biphasic reaction; the bleeding time 3 minutes; the clotting time 7 minutes. A liver-function test showed 90 per cent of the dye retained. A sugar-tolerance test showed an elevated flat curve: fasting, 78 mg. per 100 cc.; half an hour, 124 mg.; an hour, 230 mg.; an hour and a half, 200 mg. A blood fragility test was normal.

On the twelfth hospital day an exploratory laparotomy revealed a definitely cirrhotic liver with a large smooth spleen, four times the normal size, and dilated epigastric veins. An omentopexy was performed. The patient was discharged improved on the thirty-first hospital day.

Second Admission (seven years later). After discharge, the patient was reasonably well, save for a persistent pigmentation of the skin, frequent epistaxes and decreased resistance to infections. Three years before this admission the epistaxis had been relieved by cauterization of small nasal blood vessels. About four years before admission her ankles began to swell daily. There were no other signs of cardiac embarrassment. No ascites was noticed. Two years before admission the patient was treated for acute gonorrheal vulvovaginitis. She continued to be active, although on rare occasions she was forced to stop work because of extreme fatigue. For three to four months before entry, in the evenings the patient's legs were swollen up to the hips but by morning most of the edema had disappeared. Two months before entry, after a period of extensive mountain climbing and bicycling, she developed chills, fever ranging to 102 and 103°F., malaise, anorexia and night sweats, but no definite pain, cough, vomiting, diarrhea or joint trouble. This infection lasted for two weeks and then gradually subsided, with recovery of strength and spirit, so that three weeks before admission the patient returned to work. Ten days before entry she developed fatigue, and four days later, while enjoying a week-end holiday, she began to feel "dopey," feverish and nauseated. She retired to bed, and suddenly began to experience crampy pains over the abdomen, most marked below the umbilicus and associated with the passage of four to five watery stools. The diarrhea increased to seven or eight times daily, and four days before admission she had a temperature of 101.5°F. A physician found a dull, distended abdomen, with right-lower-quadrant ten-

derness and, by rectal examination, extreme tenderness of the cervix. During the three days before admission the abdominal pain increased, spread to the epigastric region and extended to the lower costal regions anteriorly, especially on the right. Alternate constipation and diarrhea began to appear.

Physical examination revealed an acutely ill, well-developed, fairly well-nourished woman. There was a generalized dirty-brown pigmentation of the skin, which was not particularly increased in the folds of the skin. Examination of the heart was negative except for a rather harsh systolic murmur heard over the precordium. The blood pressure was 120 systolic, 70 diastolic, and the aortic second sound was greater than the pulmonic second sound. The lungs showed egophony, with absent tactile fremitus and breath sounds and flatness to percussion over the right base posteriorly beneath the angle of the scapula. The abdomen was distended, tender and doughy. Splenic dullness was increased, but the edge was not felt. There were no masses or shifting dullness. There was no ankle edema. The remainder of the examination was negative.

The temperature was 99.6°F., the pulse 100, and the respirations 22.

Examination of the blood revealed a red-cell count of 3,200,000 with 10.5 gm. of hemoglobin (photoelectric-cell technic), and a white-cell count which varied from 4600 to 6700, with 60 per cent polymorphonuclears, 25 per cent lymphocytes, 11 per cent monocytes, 2 per cent eosinophils and 2 per cent basophils; the smear showed moderate achromia with moderate variation in size and shape; the platelets were normal. A blood Hinton test was negative. The urine examination was negative save for the presence of a ++ test for bile. The stools were light-brown, soft, formed and guaiac negative; no amebae were observed. A van den Bergh determination showed 7.2 mg. of bilirubin per 100 cc. of serum, with a biphasic reaction. A liver function test showed 80 per cent of the dye retained in the serum after one hour. The blood sugar was 84 mg. per 100 cc., the serum protein 5.7 gm., and the total cholesterol 191 mg. Widal and *Brucella abortus* agglutination tests were negative. Blood and urine cultures were negative.

Roentgenograms of the chest and abdomen showed that the soft tissues of the abdomen had a hazy appearance, apparently due to ascites. The kidneys, however, were faintly visible and appeared normal. The spleen was moderately enlarged. Lying at the tenth interspace on the right there was an area of calcification measuring 1 cm. in diameter, which probably represented a small gallstone. The right diaphragm was obscured by a hazy homogeneous density in the lower right chest. Fluoroscopically motion of the right diaphragm was limited. The left lung was clear. The heart shadow was transverse in position and appeared to be slightly enlarged. The appearance was consistent with fluid at the right base.

The patient's temperature, pulse and respirations fell to normal the day after admission and remained so for the seven-day hospital stay. The right chest was tapped and bloody fluid obtained, revealing 164,000 red cells and 430 white cells (mostly lymphocytes) per cubic millimeter. A fragility test was normal. The patient improved, although without known cause, and was discharged on the seventh hospital day.

Third Admission (six months later). Following discharge the patient had monthly attacks of fever lasting four to five days with temperatures ranging around 103°F., associated with pleural pain under the right or left costal margin. Two months before admission one such episode was associated with loud pericardial friction sounds, following which a rapidly progressive pericardial effusion developed that gradually subsided with Mercupurin medication. Pleural effusion regularly followed each febrile episode and never completely cleared. One month before admission a typical gallstone colic occurred, and a week later she began to complain of diffuse severe headaches. A neurological examination was negative, but a few days later a right homonymous hemianopsia was observed. The fundi were normal, however. A swaying and unsteady gait developed so that she bumped into objects in walking about her home.

Physical examination revealed definite jaundice of the skin and scleras. There was evidence of pleural effusion, but pericardial effusion was not demonstrated. The tip of the spleen was palpated to about the level of the umbilicus; it was tender, firm and smooth. The liver was palpated 8 cm. below the costal margin in the right midclavicular line. In the epigastrium just to the right of the midline there was a firm, round, tender mass that had not been observed before. A neurological examination revealed a right hemonymous hemianopsia and an unsteady gait with a positive Romberg test. Deep reflexes were stronger on the right than on the left. A lumbar puncture was negative. Roentgenograms of the skull were negative.

The temperature, pulse and respirations were normal.

The patient remained in the hospital for four

days and then was discharged home, without definite improvement.

Two weeks after discharge a lumbar puncture for increasing headaches was performed by her physician. The initial pressure was 300 mm. of water and the terminal pressure after the removal of 20 cc. of fluid was 160 mm. Following this she had no further headaches. Ascites continued to increase, with but slight diuresis following the administration of Mercupurin. Four weeks after discharge she had an acute upper-abdominal pain that lasted for one hour. She showed an increasingly rapid weight loss, in spite of persistent ascites. About five weeks after discharge she awakened one morning with a very severe frontal headache, and twenty minutes later she became irrational and vomited. She became partly comatose and developed rapid respirations, with a pulse of 48 and a blood pressure of 115 systolic, 80 diastolic. She then developed mild generalized convulsions, went into deep coma and expired about eight hours later, approximately nine years after the onset of symptoms.

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Differential Diagnosis

Dr. Wyman Richardson: This is a very complicated case but I am going to pick out a possible explanation for most of the patient's symptoms. I think if we try to explain all the symptoms we are going to get into difficulty. We can say that at the beginning of the first admission the patient had cirrhosis of the liver, and the subsequent history indicates that for a long period she got along remarkably well. From the second admission on she had increasingly severe symptoms that eventually resulted in death. The symptoms were not clearly infectious in origin, although she had had bouts of fever, and they did involve the brain terminally. It seems to me that these symptoms could best be explained on the basis of a malignant tumor. If you have a patient with cirrhosis and symptoms suggesting malignant tumor you can guess that the patient has a malignant tumor developing in the cirrhotic liver, in other words, a hepatoma.

In the first place, what about the endocrinological symptoms? We have to explain amenorrhea, pigmentation, possibly hypertrichosis, acne and a curious blood-sugar curve. I am no endocrinologist, and I am not going to get caught in any deep water on this subject, but it seems to me very difficult to put all these symptoms together on any one basis. There is not enough evidence to assume that she had a masculinizing tumor or any such syndrome. All we have is amenorrhea and hypertrichosis. If she had a masculinizing tumor we should expect the mention of changes in the breasts and of a complete shift of the body habitus toward the masculine type. Acne is common at the time of puberty. It may suggest overactivity on the part of the pituitary gland and does go with certain pituitary disorders of a primary nature. If you consider the pigmentation and the hypertrichosis as due to some endocrine disturbance, you might think of the possibility of adrenal tumor. The trouble is that pigmentation is associated with atrophy of the adrenal cortex, whereas hypertrichosis is associated with tumor of the cortex. The amenorrhea and so forth I am not going to try to put together on a primary pituitary basis. We know she had severe underlying systemic disease, probably present for a long time, and it seems better to consider that this patient's endocrine symptoms were due to a secondary disturbance of development of the endocrine glands as a result of profound underlying systemic disease. Now we come to the pigmentation, and the striking thing is that it appeared before there was any considerable amount of jaundice. If it was due to liver disease, I should expect it to have been associated with an obstructive jaundice and with a very severe jaundice, and there should have been with it symptoms which the record states that this patient definitely did not have, that is, itching of the skin. The amount of bile in the blood does not seem to be sufficient to account for this severe pigmentation in the skin. Of course, she may have had a mild jaundice over a very long time, and it may conceivably have caused pigmentation of the skin, but in such a case, I should think there would have been more pigmentation in the scleras.

If it was not due to jaundice, what was it due to? We have a patient with cirrhosis of the liver and pigmentation and what looks like a diabetic sugar curve, and in spite of the lack of glycosuria I should call it a pigment cirrhosis, in other words, hemochromatosis. I have an impression that hemochromatosis is very rare in one sex or the other, but I do not remember which; so I am all right on this so far. So let us call it pigment cirrhosis and see what happens.

The second admission is very complicated. I think it is better not to try to pick it apart. If we take the bouts of chills and fever and associate them with gallstones and possibly gallstone colic, one could call this Charcot's fever if one wished to, that is, a low-grade infection associated with biliary-tract disease. That does not explain the diarrhea. She may well have picked up an enteritis which was purely incidental. She did have a considerable amount of abdominal pain and

cervical tenderness on pelvic examination. We also know she had gonorrheal infection, and it is quite conceivable that she still had some inflammatory disease in the pelvis. The difficult things to explain and the things we have to talk about are the fluid in the chest, which was definitely bloody, and the pericardial effusion with a pericardial friction rub. Bloody fluid in the chest can be due to a pulmonary infarct, but I do not believe it is very common to get a considerable amount of bloody fluid in the chest on that basis. The commonest cause is a malignant tumor of the chest involving the pleura. In this case there was distinct blood, not just blood-tinged fluid. Of course, you can get bloody fluid from an effusion but usually it is not so bloody as this was. The whole picture could be due to infection, and we should perhaps be thinking in terms of tuberculosis. If I start talking about tuberculosis I am going to wander in a circle and rearrange this whole business, so I am going to say that the symptoms were due to malignant tumor involving the pleura and that the pericardial friction rub probably was on the same basis.

I must mention the fact that she had a systolic murmur in the heart, and therefore we have to consider the possibility of vegetative endocarditis and the throwing off of emboli to account for the chills and fever. I mention that so that I shall have spoken of it, but I do not believe that was the situation here, because we have no other evidence of embolic disturbance. The diarrhea I am going to leave alone.

Then we come to the final episode of some lesion involving the brain. Right homonymous hemianopsia — if I remember my anatomy — means a lesion somewhere posterior to the chiasm. She also had ataxia, which suggests the possibility of cerebellar involvement. I am not going to try to localize it closely because I do not see where to put it. There is no reason to suppose it was an abscess. I do not see how we have any reason to suppose it was an embolus. The onset was not sudden, but gradual. I do not believe that an embolus from the heart would have had such a gradual onset as this. Therefore, we are left with tumor, a tumor involving the brain. The liver was enlarged, and there appeared a rather firm mass in the epigastrium that was thought to be in the region of the gall bladder. Whether this was just a distended gall bladder or involvement of the omentum — the patient had had an omentopexy — or whether it was a malignant tumor I do not know, but it did help me to come to the conclusion that very likely this patient had a malignant tumor in the upper abdomen. If the mass was gall bladder it is rather in favor of tumor as against stone. We have the information that the patient had cirrhosis of the liver, and I am going to say it was hemochromatosis. I believe she had a malignant tumor, probably a primary liver tumor. As for the rest, she may have had low-grade biliary-tract infection and may have had gonorrheal infection of the pelvic organs, and the endocrine symptoms were probably on a secondary basis in a woman who had a severe underlying disease.

Clinical Diagnoses

Cirrhosis of liver, with splenomegaly and ascites.
Hepatoma, with metastases to lungs and brain.

Dr. Richardson's Diagnoses

Pigment cirrhosis of liver (hemochromatosis).
Primary tumor of the liver (hepatoma), with metastasis to lungs and brain.
Low-grade biliary-tract infection?
Pelvic inflammatory disease (gonorrheal)?

Anatomical Diagnoses

Cirrhosis of the liver, toxic type.
Hemochromatosis, early.
Hepatoma, with metastases to lungs.
Ascites.
Pleural effusion.
Operative wound: omentopexy.

Pathological Discussion

Dr. Tracy B. Mallory: The death of this patient occurred on an occasion when most of the members of the Department of Pathology were attending a meeting of pathologists in another city. The remaining man could not leave the hospital, and as a result, the autopsy was performed by a member of the clinical staff. Here is his report: "I am not much of a pathologist. I did the autopsy at an undertaking room before the body was embalmed. She had a good omentopexy. I cut into the abdomen and found dilated veins around the site of the previous operation. There was a good deal of straw-colored ascitic fluid. The pelvis was grossly negative. The ovaries and tubes appeared normal. Certainly there was no evidence of any pelvic abscess. The liver was considerably enlarged, and the left lobe, which presented in the epigastrium, contained a large mass that was necrotic and adherent to everything. By the time I got it out it was quite well broken up. The remaining liver was studded with greenish-white hard nodules. Both sides of the chest contained a lot of straw-colored fluid.

The pericardium was smooth and glistening, and contained no tumor. The heart appeared normal, and I could see no vegetations along the heart valves. The lungs were studded with masses similar to those in the liver. I did not attempt to examine the head. Both kidneys seemed large to me."

Microscopical examination showed that the tumor was a primary liver-cell carcinoma or hepatoma. In the pulmonary metastases the tumor cells were actively secreting bile into dilated canaliculi which were present between them. The liver showed a very marked cirrhosis, and besides pigmentation due to the extreme grade of bile stasis there was some further pigment. A considerable proportion of the pigment reacts with potassium ferrocyanide and is hemosiderin. So we can say there was some degree of hemochromatosis. I find myself skeptical, however, as to whether that was the primary cause of the cirrhosis because, although pigment was present in moderate amounts in the liver cells, there was almost none in the stroma. In a primary hemochromatosis the liver cells, as they die, deliver up this pigment, which is carried by phagocytes to the portal areas and then deposited in large amounts in the stroma. That condition was not present here. I think there was beginning hemochromatosis, but the original cirrhosis was something else and I have no idea what. Sections from the pancreas showed no pigment deposits.

DR. RICHARDSON: Have you a section of the skin?

DR. MALLORY: We did not get any, unfortunately. The degree of hemochromatosis of the liver was slight enough so that I think it is improbable that the skin pigmentation, which had been present for eight years, was due to iron, but I can only guess about that.

DR. EDWARD G. THORP: Dr. Chester M. Jones and Dr. William D. Smith saw the patient, and they also thought it was chronic jaundice rather than hemochromatosis that produced the pigmentation.

DR. RICHARDSON: I still think it is funny that she had pigmentation of the skin before she was deeply jaundiced.

DR. THORP: She did have jaundice in the scleras. I saw her during the last three years and the scleras were almost always yellow.

DR. MALLORY: I think we can let Dr. Richardson believe that it was iron pigment in the skin if he wishes to.

DR. RICHARDSON: Thank you.

CASE 26282

PRESENTATION OF CASE

First Admission. A thirty-nine-year-old American salesman was admitted to the hospital complaining of recurrent attacks of red, painful, swollen joints of some ten years' duration.

Eighteen years before admission at the age of twenty-one the patient suffered with an acute attack of gonorrheal urethritis which lasted three months and then cleared without residual symptoms. He had led an active healthy life for many years. Although no gourmand, he liked his food on the bountiful, rich side; his diet included meat three times a day and he often "sat down to" a pound and a half of steak at a time. It was stated that he "used a small amount of wine," never exceeding a quart a week. He took no more than ten glasses of beer a day, and one quart of prohibition-era gin weekly. While thus enjoying himself ten years before admission he had had a recurrence of the gonorrheal urethritis. It lasted only three days, and he received medical attention for it. Shortly after this — the patient did not recall the exact length of time — he was suddenly awakened out of a sound sleep with an excruciatingly painful, throbbing, red and swollen right large toe, the affected area being the metatarsophalangeal joint. He was forced to rest his foot upon a pillow, well elevated, and could not bear even the weight of a sheet over the foot. The attack was so severe that he could not sleep for the three days during which the episode lasted. When the attack subsided there was no residual pain, redness or swelling about the joints and there was no limitation of motion or other abnormality. He was well for two years following this attack, and then the same joint of the opposite foot became identically affected for three or four days. Six years before admission a third attack occurred, limited to one toe, and at the same time he noted small nodules about the periphery of the pinna of each ear. They were hard, firm, non-tender and not painful. He was able to express a whitish-yellow, semi-solid material from one of the nodules. He then experienced recurrent attacks of joint pain at more frequent intervals, and the joints involved included the metatarsophalangeal joints of the first and fifth digits of both lower extremities, and the wrists. At no time were the shoulders, elbows or knees involved. It was stated that there was no known factor which precipitated the joint attacks; trauma was not incriminated. It was stated that the patient gave a family history of gout. Six months before admission the patient had an at-

tack of epigastric pain; a physician was consulted and after x-ray studies a diagnosis of low stomach ulcer was made. The patient was placed on a Sippy regime, and his symptoms were relieved. He continued the diet for five months. Three months before entry and continuing until admission the patient experienced weekly attacks of drenching night sweats. He experienced increasing malaise and weakness and a loss of 12 pounds in weight during the five-month interval before admission. The remaining family, marital and past histories were noncontributory.

Physical examination revealed a well-developed, slightly undernourished man in no apparent distress. There was a small area of dullness posteriorly at the left apex of the chest. The heart was not remarkable, save for a soft, blowing, apical systolic murmur. The blood pressure was 140 systolic, 100 diastolic. There were a few old tophi palpable in the pinna of each ear. The remainder of the examination was negative.

The temperature, pulse and respirations were normal.

Examination of the blood showed a red-cell count of 4,500,000 with 80 per cent hemoglobin, a white-cell count of 9000 with 81 per cent polymorphonuclears, and a normal smear. Examination of the urine was negative. A urine concentration test showed specific gravities which varied from 1.018 to 1.022. Sputum examinations were negative for acid-fast bacilli. A blood Hinton test was negative, as was a complement fixation test for gonococcal antibodies. The nonprotein nitrogen was 50 mg. per 100 cc., the fasting uric acid 5.4 mg., the serum protein 6.1 gm., and the venous-blood nonprotein nitrogen 83 mg. The serum uric acid (Benedict) was 8.9 mg. per 100 cc. A prostatic smear showed no gram-negative intracellular diplococci. A phenolsulfonephthalein test of urinary excretion showed 10 per cent excretion in one half hour, and 25 per cent total excretion in one hour.

Intravenous pyelograms showed that the kidney outlines were visible on both sides. They were rather small, particularly that on the left. The secretion of the dye was somewhat slow. At no time were the pelves well outlined. On the left side the pelvis appeared to be of normal size and shape; on the right there seemed to be slight dilatation and blunting of the calyces.

Roentgenograms of the stomach and duodenum showed scar formation in the center of the duodenal cap. The rugae of the stomach appeared slightly enlarged. The chest plate showed that the diaphragm was normal in position. There was a cavity measuring 4 cm. in diameter in the right apical field, with marked mottling extending down to the third rib on this side. There was a similar cavity with a fluid level in the left lower lung field, lying posteriorly. Films of the hands showed slight soft-tissue swelling about the terminal interphalangeal joint of the left middle finger and a small area of calcification of the soft tissues near the terminal interphalangeal joint of the fourth finger on this side, without any evidence of disease in the joints. The films of the feet showed a triangular area of decreased density measuring about 1.5 cm. in width at the base of the first phalanx of the great toe on the right.

The patient remained in the hospital for about three weeks and was discharged to a county tuberculosis sanatorium.

Second Admission (five months later). The patient was admitted in a state of anxiety which had developed in close time relation with the discovery of pulmonary tuberculosis and the consequent necessity of changing from living at home to a prolonged stay in a sanatorium. At this time the urine concentrated only up to 1.008, with a slight trace of albumin and 8 to 10 white blood cells per high-power field in the sediment; the blood pressure was 150 systolic, 115 diastolic. He was given psychotherapy and re-entered the sanatorium for further care of his tuberculosis.

Third Admission (twenty months later). The patient was admitted for further study. The chest lesion had improved under sanatorium care. An ophthalmoscopic examination showed marked nicking of the veins but no exudate or hemorrhage in the fundi. The blood pressure was 196 systolic, 132 diastolic. Although he ran a slightly elevated temperature during the early days of his hospital stay, it slowly fell to normal, and he was discharged on the sixteenth day.

Final Admission (twenty-two months later). For three to four months before this admission the patient noted increasing anorexia, malaise, weakness, frequent colds and a weight loss of 15 pounds. He had been on a low-purine diet with 1/120 gr. of colchicine three times daily, but in spite of this, two days before admission, acute pain without redness or swelling developed in his knees and toes. He began to vomit and retch. Apparently as the result of frequent retching, he developed diffuse abdominal soreness in the epigastrium along the costal margins. He entered the hospital for further treatment.

Physical examination revealed a poorly developed and nourished man who retched violently but failed to vomit food or gastric contents. There was dullness and bronchial breathing at both

apices, but no rales were heard. The chest examination was otherwise negative. Examination of the heart was negative. The abdomen was equally tender in all quadrants; there were no masses. The liver and spleen were not felt. The toes and metatarsal joints of both feet were acutely tender and slightly reddened. No ear tophi were observed.

The temperature was 99°F., the pulse 100, and the respirations 20.

Examination of the blood showed a red-cell count of 3,200,000 with 62 per cent hemoglobin, and a white-cell count of 10,000 with 86 per cent polymorphonuclears. The urine showed a specific gravity up to 1.005, with a +++ albumin test and an essentially negative sediment. The stools were guaiac negative, and sputums showed no acid-fast bacilli. The blood uric acid was 11.1 mg. per 100 cc., and the blood chlorides were equivalent to 97.0 cc. of N/10 sodium chloride per liter. The serum nonprotein nitrogen was 135 mg. per 100 cc., the serum calcium 7.9 mg., the serum phosphorus 8.8 mg., and the serum phosphatase 6.1 units. The carbon dioxide combining power of the blood was 12.6 milliequiv. per liter.

Roentgenograms of the chest showed multiple areas of density in the right lung, many of which were rather sharply defined. The upper lobe was reduced in size, displacing the trachea and heart shadows to the right. There was a hazy band of density in the left lung field.

The patient continued to fail. A uremic frost appeared on his face; he lapsed into coma and expired on the twelfth hospital day, some fourteen years after the onset of joint symptoms.

Differential Diagnosis

Dr. Charles L. Short: The history of the first admission seems to be a classic story for acute gouty arthritis. With recurrent attacks involving the big-toe joint in a man, with complete clearing between the attacks, I do not believe we need to take the time to consider any other condition in differential diagnosis. The picture certainly does not suggest gonorrheal arthritis, and I think that the gonorrhea is merely an incidental finding, although the infection may have precipitated the first attack. The patient was younger than usual for the onset of gouty arthritis, but we have seen a good many patients in the twenties, and even some children. At the end of four years he apparently developed tophi in his ears, and we wonder if they were aspirated and the chemical diagnosis of gout established. From then on he had increasingly frequent attacks. The symptoms became more widely distributed, spreading so as to involve the upper extremities, but even after ten years when he came into the hospital he was apparently still having recurrent acute attacks and was not in the chronic stage with persistent joint changes.

At the time of his first admission he showed definite signs of renal impairment. I do not quite understand the discrepancies in the nonprotein nitrogen, but in any case he had retention of nitrogenous products. He had a diminished phenolsulfonephthalein test, although it is quite true that he showed no abnormalities in the examination of the urine itself and he concentrated quite well. Apparently he had increased blood pressure, although only one reading is given, and only the diastolic pressure was really high. Certainly we can say that the uric acid reading of 8.9 mg. per 100 cc. in the serum was definitely high, although, in view of his diminished renal function, this is not necessarily significant. I think we have enough to make a diagnosis of gout without this finding, and I am still curious to know whether the tophi were ever aspirated at the time of the hospital admission and a definite diagnosis made.

Shortly before this admission we run into two new sets of symptoms, one which from the history sounds very much like that of a duodenal ulcer, and the other like that of some infectious process, with the physical examination suggesting localization in the chest. I think we might show the x-ray films now, as apparently they established the diagnosis.

Dr. Aubrey O. Hampton: These films were taken on the first and second admissions. The third admission films are not here. This is the one at second examination. There is scarring in the midportion of the left lung and in the entire upper lobe of the right. I do not see any shadows which could be definitely interpreted as cavities. There are a few discrete round nodules in the lung which could be due to tuberculosis or metastatic cancer. But judging from the description of the previous films and looking at these films, I think tuberculosis is the correct diagnosis.

Dr. Short: Have you the pyelograms or the bone films?

Dr. Hampton: No.

The apex of the heart is rather blunt and appears to indicate some hypertension without much dilatation.

Dr. Short: From reading the description of the pyelograms, would you care to commit yourself?

Dr. Hampton: From reading the description,

I think one kidney is larger than the other and there is a question of clubbing of the calyces on one side. There is not much wrong with the kidneys.

DR. SHORT: It could probably all be due to impairment of function?

DR. HAMPTON: Yes.

DR. SHORT: From the x-ray findings alone we must make the diagnosis of pulmonary tuberculosis with cavity formation, in spite of the fact that the organisms were not recovered. The kidneys seemed to be small by x-ray and showed diminished excretion, which would fit in with the clinical impression of the renal situation.

To summarize thus far, this patient had had gout for ten years, had evidence of renal damage and presumably had an active duodenal ulcer and active pulmonary tuberculosis. The outstanding features in the next two admissions are the facts that his chest disease had apparently improved, that the blood pressure was rising and that he was showing signs of renal failure.

At the age of forty-three he came in for his final admission. The urine showed a poor concentration, and he had a high nonprotein nitrogen. He had acidosis and phosphate retention. He developed anemia and died, with what seems to have been uremia.

In conclusion, from the clinical findings a diagnosis of gout can be made in this patient, although we have not really an unshakable diagnosis in the absence of demonstration of urates in the tissues. I believe that he had pulmonary tuberculosis and a duodenal ulcer and that he died in renal failure, with hypertensive vascular disease. The last does bear a relation to gout, although we do not know the nature of the relation. In this patient there was no hint of previous kidney disease, such as glomerulonephritis or pyelonephritis. I will mention amyloid disease, but I do not believe we have any evidence for that. As to the nature of the renal lesion, I doubt that Dr. Mallory will be able to say that these kidneys are characteristic of gout; however, there will probably be urate deposits in them. If my diagnosis is correct, I hope he will discuss the significance of urate deposits in the kidneys in gout as the cause of renal impairment.

DR. TRACY B. MALLORY: Dr. King would you like to comment?

DR. DONALD KING: I thought that the case looked like one of tuberculosis and that we did not have to consider cancer.

DR. JOHN TALBOTT: There is one point that is not in the history but should have been. When the patient was in the army in 1917 the doctors said he had acute Bright's disease. There were no symptoms which accompanied this diagnosis at that time, and we tended to discount it because kidney changes occur so frequently in patients with gout. As to the family history, there is a brother who has developed classic gout within the past year. I think if Dr. Thannhauser were discussing this case he would say that this is an example of primary renal disease, with the gout secondary to the renal insufficiency, a theory which I am reluctant to accept. In addition to gout he had three other diseases which required treatment: tuberculosis, psychoneurosis and duodenal ulcer.

CLINICAL DIAGNOSES

Gout, acute tophacious.
Pulmonary tuberculosis, with cavitation.
Nephritis, gouty.
Duodenal ulcer, healed.

DR. SHORT'S DIAGNOSES

Gout.
Pulmonary tuberculosis.
Duodenal ulcer.
Vascular nephritis.

ANATOMICAL DIAGNOSES

Nephritis, chronic (? type).
(Uremia).
Gout, with tophi of ears and fingers, bilateral.
Pericarditis, acute fibrinous.
Pulmonary tuberculosis, bilateral, fibroid.
Tuberculous adenitis, tracheobronchial.
Pleuritis, chronic fibrous, bilateral, apical.
Cardiac hypertrophy, hypertensive type.
Cysts of kidneys, multiple.
Passive congestion of liver.
Arteriosclerosis, coronary and aortic, slight; renal, marked.
Pulmonary edema.

PATHOLOGICAL DISCUSSION

DR. MALLORY: The autopsy showed obvious gout with extensive urate deposits in the joints, also markedly diseased kidneys. The kidney on one side was quite large because of the presence of one big and numerous small cysts, which I think account for the slight deformity of the pelvis. The kidney on the other side weighed only 75 gm., and I suspect that if the cysts had been extracted from the first kidney it would have had about the same weight, perhaps not quite so small but almost. The kidneys showed very extensive vascular changes, with thickening of the intima of the smaller arteries and arterioles and hyaliniza-

tion of the glomerular tufts, changes which to my mind are entirely indistinguishable from ordinary vascular nephritis. One might begin to think about malignant vascular nephritis, if one believed the two can be separated. There were just a few, not very conspicuous, urate deposits in the kidney, not enough, however, reasonably to blame the rest of the kidney disease on them. Whether this was a primary vascular nephritis, one due to essential hypertension or the end result of an acute glomerulonephritis which he had in 1917, as Dr. Talbott suggested, I do not believe I can say. There was nothing special to suggest the last in the autopsy.

The heart was moderately hypertrophied. There was some coronary sclerosis without, however, a significant degree of narrowing, and there was very extensive and active pulmonary tuberculosis, with involvement of most of the left upper lobe, part of the right upper lobe and part of the right middle lobe.

DR. FULLER ALBRIGHT: What is your interpretation of the connection between gout and kidney disease? Is the kidney disease the cause of the gout, or the gout the cause of the kidney disease?

DR. MALLORY: I am not willing to generalize on one case.

DR. SHORT: Have you examined kidneys in which you thought the renal lesion was due to the urate deposits alone?

DR. MALLORY: I have never seen enough urate deposit to make me think it was the cause of renal insufficiency. Such other cases of gout as I have seen have also showed fairly marked vascular nephritis.

DR. TALBOTT: During the past three years, we have been particularly interested in the clearance of inulin by gouty patients. Most of our patients have shown some diminution in this function, which is now recognized as an index of glomerular activity. In a recent report* from our laboratory, 4 of 25 patients showed a marked diminution of inulin clearance and, hence, of glomerular filtration. Each of these 4 patients died within the past year from renal failure rather than from deforming gouty arthritis. Three of the 4 patients were autopsied at this hospital, and the fourth died in a hospital in a neighboring city. I mention these data because I am particularly impressed with the incidence of renal failure in gouty patients, and at the present time we are as much concerned with the status of the kidneys as we are with the condition of the joints.

DR. BERNARD M. JACOBSON: I should like to ask Dr. Talbott how many frank cases of gouty kidneys that might have led to uremia are recorded in the literature.

DR. TALBOTT: I believe that this question is unanswerable. With the gouty patients who have been autopsied in this hospital, no definite conclusion could be reached. In each patient the renal changes were distinctive but not specific for any commonly recognized type of nephritis. From the evidence at hand we are forced to conclude that many factors may be responsible for the inciting lesion in gouty kidneys; with the superimposed damage from increased excretion of sodium urate the anatomical picture is a very bizarre one.

*Coombs, F. S.; Pecora, L. J.; Thorogood, E.; Consolazio, W. V., and Talbott, J. H.: Renal function in patients with gout. *J. Clin. Investigation* 19:525-535, 1940.

The New England
Journal of Medicine

Formerly the
Boston Medical and Surgical Journal

Established in 1828

Owned by the Massachusetts Medical Society and Published under the Jurisdiction of the Committee on Publications

Official Organ of
The Massachusetts Medical Society
The New Hampshire Medical Society
The Vermont State Medical Society

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Subscription Terms: $6.00 per year in advance, postage paid, for the United States; Canada, $7.04 per year; $8.52 per year for all foreign countries belonging to the Postal Union.

Material for early publication should be received not later than noon on Saturday.

The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston, Massachusetts.

HARVARD SCHOOL OF DENTAL MEDICINE

Beginning in the fall of 1941, Harvard University, aided by very generous grants from the Carnegie Corporation, the Rockefeller Foundation and the Marble Foundation, will inaugurate a new five-year course in dental education with the avowed purpose of giving the future dental graduate a wider and deeper knowledge of medicine and thus a more favorable background for the study of the essential causes of oral disease. This would seem to be a highly desirable proposal.

The profession of dentistry has over a period of years developed reparative procedures to a degree of precision and ingenuity that is admired by all and valuable to many. Yet the real solution of the problem of dental care lies not so much in repair and reconstruction as in the discovery of the causes of dental disease and the prevention of abnormal conditions. It has been stated on good authority that those dentists now in practice can care for but 20 per cent of the total population. It is very unlikely that the present type of dental care can be so increased as to provide for the remaining 80 per cent, and it would thus seem that without sacrificing the skill and technical expertness attained under the present methods of education such a school as that now proposed by Harvard University could graduate each year a group of broadly trained men with both M.D. and D.M.D. degrees who could undertake, with some degree of success, the solution of the basic problems involved and thereby reduce the need for reparative and reconstructive dentistry. Furthermore, the association of dental and medical students in their basic preclinical and clinical subjects should bring to the medical graduate a knowledge of oral medicine and oral disease that is now, unfortunately, lacking in their training, and to the dentist a knowledge of internal medicine that could be of inestimable value to him.

NEUROLOGY

Neurology as a special department of medicine was inaugurated about one hundred years ago by Romberg. He wrote the first textbook and had the first definite department for diseases of the nervous system, other than psychiatric, in a general hospital. The subject evolved slowly through the efforts of the great French neurologist, Charcot, and his associates and subsequently by the work of their English colleagues, Hughlings Jackson and Gowers. Charcot never found time to write a great textbook, although his contributions to the literature of neurology are extensive. They are mostly in the form of clinical lectures as taken down by his students, supplemented by individual papers in neurological and other journals. Hughlings Jackson also wrote innumerable papers, but never put his ideas into a textbook. Gowers, however, in the nineties wrote one of the great textbooks on neurology, far greater than any up to its time and perhaps as great as any that has ever been written. It was a personal textbook, giving his experiences of many years in caring for patients with neurologic dis-

orders. In addition he read widely into the literature of his time. A book of a slightly different character, and more comprehensive, was published by Oppenheim in Berlin in 1894. Known throughout Europe, the book also became a favorite with English-speaking physicians, for there was an excellent English translation of the fifth edition by Alexander Bruce, of Edinburgh. These two books have held the field in an undisputed manner up until the present time; although there have been literally hundreds of other books, nothing has ever been written to compare with them. That of Oppenheim was the more scholarly of the two, with extensive reference to the periodical literature. The book, however, was not quite so personal as that written by Gowers, and although it forms an excellent reference book even today, it did not have the fine touch exhibited in the volume by his colleague in London.

Recently there has come to hand another book, a great textbook of neurology, eminently fitted to be classified in the same category as those written by Gowers and Oppenheim. This is the two-volume text by the late Dr. S. A. Kinnier Wilson,* edited and put into final form by his old friend, Dr. A. Ninian Bruce, the son of the Edinburgh physician who translated the German book by Oppenheim for English-speaking students. Wilson, backed by an enormous clinical experience, combined all the fine clarity of thought so observable in Gowers's textbook with the scholarly reference attitude characteristic of Oppenheim's publication. Written in a frank, straightforward manner, Wilson saw fit to separate the wheat from the chaff in his selected list of references and appears not to have missed any contribution of importance in the periodical literature. Moreover, he obviously evaluated every paper, and in instances where he did not approve, although he thought the observation important, he did not hesitate to say so. This attitude is in every way characteristic of the man, for a more honest, straight-thinking individual could not have been encountered. The completeness of his references, moreover, speaks highly for the efficiency with which he examined the literature. Papers of moderate or even minor importance are referred to if there was even one point that appealed to Wilson. All the great names in neurology of the past forty years are mentiond, and in addition, one finds innumerable references to men of lesser importance. In completeness this book could hardly be improved upon. Its importance lies, however, not only in its completeness but in the endeavor of the author to evaluate the material and express his opinion in a clear-cut manner.

*Wilson, S. A. K.: *Neurology*. Edited by A. Ninian Bruce. 2 vol. 1838 pp. London: Edward Arnold & Co., 1940.

Like all textbooks, of course, it lags a little behind the times. Advances are being made so rapidly in neurology that no textbook could possibly be up to date when it is issued. This book covers the period up to 1937 or thereabouts, but one misses the latest advances, such as the use of potassium in familial periodic paralysis, Prostigmine in myasthenia gravis and Dilantin in epilepsy. Surgical procedures that are now well accepted, such as operation for a ruptured intervertebral disk, are, naturally, only briefly mentioned. After one reads some of the chapters, however, it seems that perhaps such unavoidable omissions are not so important as they appear to be at first sight.

Wilson carried out the biblical admonition to "hold fast to that which is good," and for this splendid attitude the medical profession owes him a debt of gratitude. He added to the field of medicine a text of fundamental importance, and quite possibly the last book of its type that will ever be written. The subject of neurology is growing so rapidly that one cannot keep a textbook either up to date or, if a complete résumé of recent advances is added with each new edition, within the bounds of two large volumes. As in other branches of medicine, monographs on single subjects will be the books of the future. The work of this great pioneer investigator is possibly the final report on neurology as a whole. No one was better fitted to evaluate the subject than was Wilson.

MEDICAL EPONYM

Cheyne-Stokes Breathing

In the *Dublin Hospital Reports and Communications in Medicine and Surgery* (2:216-223, 1818), John Cheyne (1777-1836), professor in Dublin, reported "A Case of Apoplexy in Which the Fleshy

Part of the Heart was Converted into Fat." He wrote:

> For several days his breathing was irregular; it would entirely cease for a quarter of a minute, then it would become perceptible, though very low, then by degrees it became heaving and quick, and then it would gradually cease again: this revolution in the state of his breathing occupied about a minute, during which there were about thirty acts of respiration.

William Stokes (1804–1878), physician to the Meath Hospital, reported his "Observations on Some Cases of Permanently Slow Pulse" in the *Dublin Quarterly Journal of Medical Science* (2: 73–85, 1846). He quoted Cheyne's description of this type of breathing and described a patient of his own who was similarly affected.

> For more than two months before his death, this singular character of respiration was always present, and so long would the periods of suspension be, that his attendants were frequently in doubt whether he was not actually dead. Then a very feeble, indeed barely perceptible inspiration would take place, followed by another somewhat stronger, until at length high heaving, and even violent breathing was established which would then subside till the next period of suspension. This was frequently a quarter of a minute in duration. . . .

R.W.B.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY*

RAYMOND S. TITUS, M.D., *Secretary*
330 Dartmouth Street
Boston

FATAL PNEUMONIA IN PREGNANCY, COMPLICATED BY MENINGITIS

Mrs. M. B., a thirty-five-year-old primipara, approximately thirty weeks pregnant, was first seen in the office on April 8, 1933. She complained of a pain in the left shoulder and of having had a cold for a few days. The temperature was 99.8°F., and the pulse 100. She was sent into the hospital immediately.

The family history was non-contributory. The patient gave a history of the usual children's diseases, scarlet fever, typhoid fever, and appendicitis at the age of eight without operation, which was followed by jaundice six months later. The tonsils and adenoids had been removed. Catamenia began at thirteen, were regular with a twenty-eight-day cycle and lasted five or six days. The last normal period had begun on September 20, 1932, making the expected date of confinement June 28.

Physical examination on admission showed a well-developed and well-nourished woman lying in bed, obviously febrile and complaining of pain in the lower left side. The throat showed moderate injection and slight edema. There was no stiffness or rigidity of the neck. Chest expansion was diminished on the left side, and there were rales over the left lower base, extending upward to the lower border of the scapula. The right lung was clear and resonant. The heart was not enlarged; there were no murmurs. The blood pressure was 112 systolic, 60 diastolic. The abdomen was soft. The uterus was enlarged to a size compatible with a pregnancy of seven and a half months; the fetal heart was heard. No rectal or vaginal examinations were done. The extremities were negative. A diagnosis of pneumonia was made, and a medical consultation was immediately held.

The white-cell count was 12,100. A blood culture and the sputum showed Type 4 (Group 4) pneumococci. An x-ray film showed an inflammatory process involving the lower portion of the left lung with a small amount of fluid.

The temperature vacillated from 99 and 103°F. for the first four days; the pulse ranged between 90 and 140, and the respirations were 30. On April 13 the temperature came down to normal, rising only to 100°F. It remained normal for the next two days, and it seemed as if she were improving.

On April 16, after having had irregular uterine contractions for forty-eight hours, a female child was born normally. The baby weighed 2 pounds, 13 ounces, and lived twenty-four hours. Following the birth, the patient's temperature rose to 103.2°F. but came down to 100 and remained there for the next few days. The white-cell count on April 16 was 32,000.

On the morning of April 18 the temperature was 100°F., and the pulse 90. The patient complained of pain and stiffness in the neck. A positive Kernig sign suggested meningeal involvement. A lumbar puncture was done, which confirmed the diagnosis of meningitis, turbid fluid being found; bacteriological examination showed the presence of pneumococci. That afternoon the temperature rose to 104°F., and the pulse to 130. The patient became rapidly worse, the temperature rising to 106°F., and the pulse to 150, and she expired on April 19.

Autopsy showed bronchopneumonia of the left lung, left empyema, interlobar abscess, mediasti-

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

nal abscess, acute endocarditis and purulent meninigitis.

Comment. Pneumonia in pregnancy must always be looked on as a very serious complication. In 1933 many types of pneumococci now specifically recognized were put in the large group of Type 4, for which there was no serum available. The treatment was symptomatic and supportive. It has never been considered advisable as a therapeutic procedure to induce labor in cases of pneumonia. It was recognized then that not infrequently pregnancy associated with pneumonia might be terminated normally by miscarriage or premature labor because of the prolonged fever and extreme toxemia. In this case the temperature having come down to normal it was hoped that the pregnancy might be saved; however, labor started spontaneously. The delivery was simple and uncomplicated. The extension into the meninges was not looked for and proved to be a fatal complication.

Chemotherapy might well have saved this patient's life. Nowadays it is customary as soon as pneumonia is diagnosed to start sulfapyridine even before the result of typing has been reported. In cases of pregnancy it is considered advisable to give sulfapyridine early and then serum if the type is known to be amenable to serum therapy. Sulfapyridine should only be administered under adequate medical supervision.

This patient's history suggested the possibility of contagion, in that she visited a pneumonia patient three days before she developed the disease herself. It is wise to remember that in pregnancy some patients are more susceptible to infectious diseases, and it is best to be extremely conservative in an attempt to avoid infection.

DEATHS

DARLING — Arthur E. Darling, M.D., of Lynn, died June 19. He was in his sixty-third year.

Born in Auburn, Maine, his early education was received there. He attended Bates College and received his degree, cum laude, from Harvard Medical School in 1906. From 1906 to 1907 he served as house officer at the Lynn Hospital.

Dr. Darling was a fellow of the Massachusetts Medical Society and the American Medical Association, and was a member of the Lynn Medical Fraternity.

A nephew and a sister-in-law survive him.

ELLIOT — Henry L. Elliot, M.D., of Salem, died June 27 in Thomaston, Maine. He was in his sixty-seventh year.

Born in Thomaston, Maine, he attended the local schools there and received his degree from Bowdoin Medical School in 1898. He served his internship at the Salem Hospital and was associated with Dr. Hardy Phippen for twelve years before starting private practice. He became a member of the staff of the Salem Hospital in 1902.

Dr. Elliot was a fellow of the Massachusetts Medical Society and the American Medical Association.

A son, a daughter and three brothers survive him.

MISCELLANY

MIDDLESEX UNIVERSITY SCHOOL OF MEDICINE

The degree of Doctor of Medicine was conferred on forty-six students of Middlesex University School of Medicine at commencement exercises on June 10, in Waltham. The following seniors received their degrees cum laude: I. Jacques Yetwin, of Elizabeth, New Jersey, B.S. Rutgers University, S.M. University of Chicago; Simon Coren, of Boston, Middlesex College; Theodore Echlov, of Boston, A.B. Harvard University; Everett Radovsky, of Fall River, B.S. Rhode Island State College. Dr. Yetwin also received the Sebrenik Prize for the student with the highest scholastic record during the four years.

The Committee on Faculty of Middlesex University has announced the appointment of Dr. J. Richard Weissenberg to a full-time teaching position for a term to commence August 15 in the medical school as professor of histology. Dr. Weissenberg is now acting curator of the Department of Microscopic Preparations in the Wistar Institute of Anatomy and Biology, where he was appointed a research fellow in 1938. Born in Germany, he received his M.D. from the University of Berlin, where he was a member of the staff of the Anatomical-Biological Institute from 1906 to 1933. He became privatdozent of anatomy in 1913, and served on the medical faculty of the University of Berlin from 1922 to 1933 as professor of histology and embryology. He came to the United States in 1937, and was appointed visiting professor of cytology at Washington University School of Medicine, where he taught histology until his Wistar appointment. Dr. Weissenberg is the author of a German textbook in embryology, and is well known for his achievements in the field of research.

CORRESPONDENCE

NAVY MEDICAL CORPS

To the Editor: Doctors are urgently needed for the United States Navy to bring its permanent medical corps to full, peace-time strength.

Examinations for appointments as commissioned officers in the Medical Corps are to be held on August 19, 1940, at the Naval Hospital, Chelsea, and various other naval hospitals throughout the country. Applicants for appointment must be male graduates of a Class A medical school, have completed an internship in a recognized hospital, be less than thirty-two years of age at the time they receive their commissions, be citizens of the United States, and be physically and professionally qualified. Professional qualifications must be demonstrated by competitive written, oral and practical examinations embracing the subjects of general medicine, general surgery, obstetrics and gynecology, preventive medicine and medical jurisprudence.

The pay, including allowances, for the newly appointed medical officer is $2699 per year if he has no dependents, and $3158 per year if he has dependents.

Applications must be completed and received at the Navy Department prior to August 1, 1940, in order to appear for the August 19 examination. Additional informa-

tion may be obtained by addressing a letter to the Bureau of Medicine and Surgery, Navy Department, Washington, D. C.

JOHN L. NEILSON,
Captain, M. C., U. S. Navy,
District Medical Officer.

Navy Yard,
Boston.

DISTRIBUTION OF BOOK ON CANCER TO MASSACHUSETTS PHYSICIANS

To the Editor: The Massachusetts Department of Public Health, through a grant from the United States Public Health Service, has recently forwarded to all physicians in the State a book, *Cancer: A manual for practitioners,* which has been prepared by a group of specialists and edited by Dr. Channing C. Simmons.

The department endeavors to keep its mailing list of physicians up to date, but there is always the possibility that a small number will be omitted due to change of residence. Any physician who has not been receiving department literature is requested to communicate with the Division of Adult Hygiene, 100 Nashua Street, so that he may receive a copy of the book on cancer.

PAUL J. JAKMAUH, M.D.,
Commissioner of Public Health.

State House,
Boston.

RESTORATION OF LICENSE

To the Editor: At the meeting of the Board of Registration in Medicine held June 27, there was restored to Dr. James B. Ryan, 53 Maple Street, Easthampton, Massachusetts, his license which had been suspended on June 6, 1940.

STEPHEN RUSHMORE, M.D., *Secretary,*
Board of Registration in Medicine.

State House,
Boston.

REPORTS OF MEETINGS

BOSTON ORTHOPEDIC CLUB

A regular meeting of the Boston Orthopedic Club was held at the Boston Medical Library on April 8, with Dr. Dennis O'Connor, of Yale University School of Medicine, speaking on "The Orthopedic Aspects of Radium Poisoning."

Dr. O'Connor recounted the history of the luminous watch-dial painters' epidemic from 1924 to 1930; he explained the technic responsible for the poisoning in this country in contrast to that in Europe. At first only the serious and fatal instances of osteomyelitis and anemia were diagnosed, but subsequent investigation revealed many more clinical and subclinical cases. The mode of entrance for the radio-active materials appears to be largely by ingestion (Martland), although Drinker and his associates consider inhalation an important source. The change of technic in 1927 prevented many new cases, but some danger still persists. A more recently recognized hazard is that of the mixers of the radio-active elements, who inhale relatively large quantities of the dust. Precautions against this danger are now being taken.

Dr. O'Connor stated that 90 per cent of the ingested radio-active materials were excreted in three to six days, and he suggested that the form of the compound, namely the insoluble radium sulfate, explained this rapid depletion and the long period before symptoms occurred in many cases. Although the method of fixation within the body is not certain, Martland has suggested that the active elements are phagocytized and then deposited in the reticuloendothelial system, particularly in the bone marrow. It has been demonstrated that 2 microgm. of active material may prove fatal. Some patients exhibited as much as 180 microgm. in the body.

The effects of such poisoning may be a local necrosis of bone and a systemic reaction in the bone marrow, consisting first of stimulation, then of overstimulation and finally of exhaustion of the blood-forming functions. The local effect may be lacking in frequently repeated small exposures. The marrow changes result in an initial leukocytosis of moderate degree followed at varying intervals by depression of the erythrocytes and leukocytes and death, usually from anemia or overwhelming infection. A certain number of patients have developed osteogenic sarcoma, presumably as a result of the constant stimulation.

Dr. O'Connor suggested that oral hygiene may be an important deterrent to the lodging of particles around the teeth, but that there appears to be some constitutional factor in the resistance to radium poisoning. Only about 20 per cent of the exposed watch-factory workers were found to have consistent electroscopic evidence of radio-active substances after being separated from the source of poisoning. Since methods at that time were relatively inadequate, it was believed that others may have felt the effects without showing definite evidence of the presence of such substances in the body.

The speaker cited typical cases, at orthopedic clinics, of radium poisoning with characteristic arthritic complaints some months or years after variable exposure to the active elements. The onset of symptoms was often related to minor trauma, but roentgenograms revealed areas of focal atrophy and necrosis, particularly near the head of the humerus and the neck of the femur. The treatment consisted of general supportive measures and physiotherapy. The diagnosis should be considered in differentiating metastatic carcinoma, chronic osteomyelitis, multiple myeloma and Ewing's tumor.

The discussion was initiated by Dr. William T. Salter, who discussed certain metabolic aspects of the disease. The radio-active elements behave like other heavy metals in their relation to calcium, and it is conceivable therefore that ammonium chloride, parathormone and tremendous doses of vitamin D might result in mobilization and excretion of these elements. The percentage which can be thus removed is probably negligible, however. Radium is first distributed throughout the tissues but finally concentrates in the bone trabeculae where it stimulates the marrow. It was emphasized that the marrow picture is one of spotty necrosis and compensatory hyperplasia, even when the peripheral blood shows evidence of aplastic anemia. Dr. Salter emphasized the early phase of stimulation and leukocytosis, which is similar to that observed in cases of benzol poisoning and is not generally recognized.

Dr. Channing C. Simmons warned of the dangers of radium water for the treatment of arthritis, and of Thorotrast and similar compounds for visualization of the blood vessels and the reticuloendothelial system. Six patients seen at the Collis P. Huntington Hospital were reported, with 3 dying of osteogenic sarcoma and only 1, who had taken radium water, living and well.

Dr. Frank R. Ober cited a case of radium poisoning in which death supervened almost twenty years after the

taking of radium water. Original assays reported no demonstrable activity of dangerous proportions in the water.

Professor Robley Evans, of the Massachusetts Institute of Technology, reminded the audience of the increasing danger of all sorts of nostrums whose existence is protected by the mere statement of their active content. Another source of such poisoning may be the products of the cyclotron and other high-speed particles that have the essential properties of the responsible alpha particles of radium. Another interesting speculation concerns the heirs of those exposed, for it is known that rats descended from poisoned parents develop a higher percentage of sarcomas than do controls. In regard to the high percentage of elimination, Dr. Evans stated that the insolubility does not appear to be a factor, since the soluble radium chloride has the same properties. Furthermore, the jaw is equally affected when the portal of entry is other than oral. Measurements indicate that the thermal energy which is equivalent to the radio-active energy dissipated is less than one millionth of a calorie per hour per gram of bone. This is about 0.25 r per day, or less than is absorbed by the usual roentgenologist, in the form of radiation energy. The minimal toxic dose appears to be about 1 microgm., for slightly more than this has proved fatal, while somewhat less has not affected clinically several people who have been known to harbor that amount for four to twenty years.

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NOTICES

ANNOUNCEMENT

CHARLES SPIVA, M.D., announces the removal of his office from 189 Bates Street, New Bedford, to 177 Nash Road, New Bedford.

ANNUAL MEETING OF EYE AND EAR SPECIALISTS

The American Academy of Ophthalmology and Otolaryngology will hold its forty-fifth annual convention in Cleveland, October 6 to 11, with headquarters at the Hotel Cleveland.

The Academy, an organization of more than 2500 specialists in diseases of the eye, ear, nose and throat, carries on an active program of education for its members. In addition to scientific papers, an elaborate series of courses is presented at each convention to bring the members up to date in their chosen fields. More than a hundred of these teaching lectures will be offered this year.

Immediately following the Academy meeting, there will be a Pan-American Congress of Ophthalmology, October 11 and 12, which eye specialists from all the Latin American countries are expected to attend.

Additional information in regard to these meetings may be obtained from Dr. William P. Wherry, 1500 Medical Arts Building, Omaha.

SOCIETY MEETINGS AND CONFERENCES

SEPTEMBER 2–6 — American Congress of Physical Therapy. Page 862, issue of May 16.

OCTOBER 6–11 — Annual meeting of Eye and Ear Specialists. Notice above.

OCTOBER 8–11 — American Public Health Association. Page 655, issue of April 11.

OCTOBER 11, 12 — Pan-American Congress of Ophthalmology. Page 898, issue of May 23.

OCTOBER 14–25 — 1940 Graduate Fortnight of the New York Academy of Medicine. Page 938, issue of May 30.

OCTOBER 21 — American Board of Internal Medicine. Page 369, issue of February 29.

JANUARY 4, 1941 — American Board of Obstetrics and Gynecology. Page 1064, issue of June 20.

APRIL 21–25, 1941 — American College of Physicians. Page 1065, issue of June 20.

DISTRICT MEDICAL SOCIETY

MIDDLESEX NORTH

JULY 31.

OCTOBER 30.

BOOK REVIEWS

A Treatise on the Surgical Technique of Otorhinolaryngology. Georges Portmann. Collaborators: H. Retrouvey, J. Despons, P. Leduc and G. Martinaud. Translation by Pierre Viole, M.D. 4°, cloth, 675 pp., with 474 illustrations and 2 colored plates. Baltimore: William Wood & Co., 1939. $12.50.

This book presents a graphic record of the various surgical technics in otolaryngology as employed by Professor Portmann in his clinic at Bordeaux.

Each procedure is briefly discussed as to indications, contraindications and preoperative and postoperative treatment. The excellent illustrations are so arranged that the reader occupies the position of the operator, and the step-by-step process of each technic can be easily followed without changing the position of the book.

Several of the procedures shown are little, if at all, used in this country, for example, the opening of the endolymphatic sac for vertigo, the three-stage operation for total laryngectomy and the trans-septal approach to the sphenoid.

As the record of a master surgeon in his field and as the source of much valuable anatomical information, this book should find interested readers among all of those who carry out operative procedures in and about the upper air passages and ears.

The Social Function of Science. J. D. Bernal, F.R.S. 8°, cloth, 482 pp., with 2 charts. New York: Macmillan Co., 1939. $3.50.

The conclusions reached by Professor Bernal are so striking that even at the risk of warping their meaning, some of them must be removed from their context and quoted.

"We now see that though capitalism was essential to the early development of science, giving it, for the first time, a practical value, the human importance of science transcends in every way that of capitalism, and indeed, the full development of science in the service of humanity is incompatible with the continuance of capitalism." Toward this unique conclusion the author builds up a strong case, indeed, through some four hundred closely packed pages thoroughly buttressed with documentary evidence. Tracing first the historical development of science, then the chaotic muddle into which science has fallen as a result of its impacts with nationalism, capitalism and war, he then attempts the most difficult task of all, the problem of the re-organization of science to best serve all human needs.

To these ends, he would reorganize the training and selecting of young scientists, the science curriculums of schools and colleges, the administration and control of research to eliminate the present wasteful inefficiency, the publication and dissemination of information, the coordination of private and public projects in science. In fact, he would tear down the present outmoded structure of science and build one in keeping with the ideals of social service. In financing such an edifice, however, while still retaining for science its vaunted freedom, Professor Bernal finds no satisfying answer under capitalism. To reach its full effectiveness, science requires "a society economically organized so that general human welfare,

and not private profit and national aggrandizement, is the basis of economic action." In Russia, he finds the only planned and integrated science serving "human needs, either directly or indirectly, and not increasing the profitability of production," and spending, in 1934, 1 per cent of the national income for the projects of science, "a sum relatively three times as great as that spent in the U. S. A. and ten times as great as that spent in Britain."

Starvation, disease, industrial slavery and war are all "remedial evils, and no one can feel that science has been properly applied to human life until they are swept off the face of the earth."

Thus, does the author deliver the charge against science which, in a time of unparalleled scientific innovation, cannot fulfill its social function under the stern hand of the profit motive, and yet has within itself all the necessary qualities to do so. But, it will "change and develop and in doing so will cease to be a special discipline of a selected few and become the common heritage of mankind."

Professor Bernal has produced a thought-provoking book, written simply, convincingly, dispassionately and painstakingly. In fact, he would have presented a more powerful plea to those unfamiliar with the intricacies and complexities of modern science had he left much of the painstaking detail for those already in sympathy with his views, and confined himself to the major task of proving to the non-scientist that science is "the chief factor in fundamental social change." But he had a mission to fulfill and seemed to believe that every shred of evidence must be presented. It is a book every thoughtful person should read.

This book is all the more important since it comes from the pen of a distinguished scientist; and scientists, unfortunately, are usually the last to recognize that there are such things as impacts of science on the social order.

How to Counsel Students: A manual of techniques for clinical counselors. By E. G. Williamson. First edition. 8°, cloth, 562 pp. New York and London: McGraw–Hill Book Co., Inc., 1939. $3.75.

The subtitle describes this book as "a manual of techniques for clinical counselors." The clinical counselor is viewed by the author as a personnel specialist in a school, college or university whose function is to counsel students with regard to problems of scholastic, social, occupational or other personal adjustments. The counselor is expected to refer the student to other specialists whenever a need for remedial teaching, occupational placement or psychiatric or other medical treatment is discovered.

The author stresses the need for professional counselors possessing not only a considerable amount of training and practical experience but also a high degree of native tact and social perceptiveness. But he also emphasizes the desirability of a "clinical point of view" on the part of all educators which recognizes the importance of individual student adjustment as opposed to the mere attainment of the traditional academic goals; and the book should prove valuable to anyone whose occupation brings him in contact with student problems, from the classroom teacher to the school doctor.

Emphasis is placed on the need for thorough diagnosis, aiming to discover the real causes of the difficulty the student is experiencing, prior to attempts at remedy. Mental tests are looked on as providing valuable data, to be combined with other observations in arriving at a diagnosis, rather than as diagnostic in themselves.

The greater part of the book is devoted to methods of approaching specific types of personal-social, educational, vocational, financial and health problems. Special chapters are devoted to speech defects, family conflicts, ineffective study habits, reading disabilities, unwise vocational choices, student self-support and a wide range of similar topics. Each chapter contains a considerable list of selected references.

Essentials of Fevers. Gerald E. Breen, M.D., Ch.B. (N.U.I. Dub.), D.P.H., D.O.M.S. (R.C.P.Lond., R.C.S.Eng.). 12°, cloth, 273 pp., with 24 illustrations. Baltimore: Williams & Wilkins Co., 1939. $3.00.

Despite the old-fashioned sound of the title,—it is so long, in this country, since the word "fevers" has carried any generic significance,—this is a thoroughly up-to-date book. The first four chapters are concerned with the general features of infection, immunity, serums and serum reactions, the spread and control of infection, epidemiology, and the examination and treatment of "fever" patients. Then follow discussions of specific diseases—diphtheria, typhoid fever, dysentery, gastroenteritis, variola and varicella, cerebrospinal fever and poliomyelitis, measles and pertussis, rubella and mumps. It is a pocket-sized volume, so that brevity was necessary; nevertheless the "essentials" which Dr. Breen aimed to furnish are certainly all there. He is sound and modern, and the book, like those written by most Englishmen, is pleasantly readable. It was designed primarily for the student and young practitioner and serves its purpose admirably. It should prove equally valuable to the older man who wishes to brush up on recent developments.

Dr. Colwell's Daily Log for Physicians: A brief, simple, accurate financial record for the physician's desk. 4°, cloth, 36-line volume. Champaign, Illinois: Colwell Publishing Co., 1939. $6.00.

This is a well-organized single-volume business record capable of handling thirty-six patients daily, providing space for the names of patients, the services rendered, the charges and the cash receipts. At the end of each month there is a summary of business done and two expense sheets for deductible and non-deductible charges, which taken together give a profit-and-loss statement. There is a personal account record for non-professional receipts and disbursements. There are special sections for records of inoculations, narcotics dispensed, obstetric cases, surgical operations, notifiable diseases and deaths. There is a space provided for calculation of the social security tax for employees, and there is a page and half a month which can be used for special purposes.

The annual summary found at the end of the year provides a résumé of the year's business, which, if properly kept, will show legitimate deductions and total income from practice and from outside sources and furnish the basic amounts needed in the estimation of income taxes.

This record book should prove invaluable to those who do not have full-time secretaries, and even secretaries should find it of use in their work.

Bacterial Metabolism. By Marjory Stephenson, Sc.D. 8°, cloth, 391 pp., with illustrations and tables. London, New York, and Toronto: Longmans, Green and Co., 1939. $7.50.

The first edition of this book appeared ten years ago as one of the *Monographs on Biochemistry* series. The author now believes, and an examination of the book supports her view, that, due to rapid developments in several dif-

ferent directions during the last decade, it no longer seems advisable to treat in monograph form a subject as broadly developed as bacterial metabolism has become.

Miss Stephenson has written an excellent and critical summary of practically all the old, as well as the recent, contributions bearing on the subject of bacterial metabolism. It is readable, informative and stimulating. There is comparatively little in the book which is beyond the grasp of one with the usual biological training who is familiar with the fundamentals of general inorganic and elementary organic chemistry. Readers with this background should not be discouraged, for example, by the few pages in the introduction which deal with energy relations — for to them the remainder will be quite comprehensible.

Three chapters on the breakdown of polysaccharides, hexoses and proteins follow consideration of bacterial respiration. Those on the latter subject and the fermentation of the hexoses are particularly well written and present this extremely complex matter in such a way as to emphasize the similarities between these processes in the single cell and those in the higher forms of life. Actually many of the facts derived from the study of the unicellular group have greatly assisted in the more difficult investigation of analogous reactions among the metozoa.

After a brief exposition of the known factors in the metabolism of nucleic acid and its derivates, the very recent and most fascinating developments in the field of bacterial nutrition are presented. These again definitely have served to reveal the close relation between the nutritive requirements of certain bacteria and those of the animal kingdom. It is perhaps to be regretted that this chapter was printed at a time when a veritable deluge of papers relating to this subject has occurred. We have known for some time of the dependence of several species of bacteria upon cozymase, vitamin B_1 and nicotinic acid, and the author's discussion of their role is entirely adequate; but the importance of vitamin B_2, pantothenic acid and other growth factors has only been recognized since the book was written, and we have every reason to believe that additions of equal significance will soon be made.

Other chapters summarize the known facts in respect to photosynthesis and the fixation of atmospheric nitrogen. Of great interest is the section dealing with the assay of enzymes which enable various micro-organisms to attack so many complex substances. Equally significant, perhaps, is the remarkable capacity of these forms when grown in mediums containing a new or unusual substrate to adapt their enzymatic processes in such a way that substances which at first are attacked to a minimum degree or not at all are eventually efficiently utilized as a source of energy or nutritive material. Such studies as those of Dubos and others on specific enzymes which hydrolyze some of the pneumococcal type-specific polysaccharides afford interesting examples of this sort of behavior and serve to indicate the practical contributions which this field of investigation may make to medicine.

The book will be read with profit by the bacteriologist and the general biologist, whereas to the increasingly large group of biochemists who recognize in the bacteria an exceedingly convenient means of investigating the reactions of living things it should prove an indispensable handbook.

An Introduction to Medical Mycology. By George M. Lewis, M.D. and Mary E. Hopper, M.S. 4°, cloth, 315 pp., with 71 illustrations. Chicago: Year Book Publishers, Inc., 1939. $5.50.

This brief textbook is the outgrowth of lectures on mycology to postgraduate students in dermatology. It deals largely with clinical and laboratory diagnoses of the common skin infections encountered in New York City, but it should prove useful over much of the United States, although the relative frequency of the various infections treated will vary considerably in other cities. The authors state in the preface, "The bibliography is not complete. It contains articles which we think important for their originality and their value in teaching. The majority of the references concern articles available in English." The reviewer would differ considerably as to the importance of many of the references included. Either the authors have lacked access to much of the important recent literature in this field, or their judgment is biased by local considerations. The book contains a large number of photographs of lesions and of a few of the commoner organisms, mostly well chosen and well reproduced.

In the first part of the book, immunological and allergic phenomena are well reviewed, apparently with considerable first-hand information. The clinical aspects and therapeusis of the superficial mycoses are adequately considered. The deep mycoses, such as coccidioidal granuloma, blastomycosis, sporotrichosis and so forth, are rather sketchily presented, as apparently they are less common in the northeastern part of the United States than elsewhere.

The second part dealing with laboratory methods is complete and well presented. Brief descriptions of the morphology and cultural characteristics of thirty-two of the commoner pathogenic fungi are included, as well as notes on the morphology of a few of the common contaminants often encountered in cultures from the skin.

You and Heredity, Including an Original Study of the Inheritance of Musical Talent. By Amram Scheinfeld, assisted in the genetic sections by Morton D. Schweitzer, Ph.D. 8°, cloth, 421 pp., with 4 color plates and 75 drawings, maps and diagrams. New York: Frederick A. Stokes Co., 1939. $3.00.

This is an extraordinarily interesting and instructive book which gives an account of the main facts of heredity. Essentially written for laymen, it may be strongly commended to those who already have an acquaintance with the subject matter. There are few people, in or out of the profession, who would fail to profit in one way or another by a careful reading of the book.

There are forty-three chapters, written in an engaging style. These are adequately illustrated.

Dr. Morton D. Schweitzer, research geneticist at Cornell University Medical College, assisted in the genetic section. An appendix offers an account of the highlights in the history of genetics and is followed by a list of books and leading publications dealing with heredity, as suggestions for further reading.

Treatment of Some Common Diseases (Medical and Surgical). By various authors. Edited by T. Rowland Hill, M.D. (Lond.), M.R.C.P. (Lond.). 8°, cloth, 398 pp., with 90 illustrations, and tables. Baltimore: William Wood & Co., 1939. $5.00.

This book covers a wide variety of subjects too numerous and diverse to enumerate. There are articles on medicine, surgery, obstetrics, pediatrics and roentgenotherapy. It is the type of book that one may pick up and read at random. There is no particular continuity in content. The factual material is, on the whole, concise and authoritative, although some of the articles are fragmentary and others extend beyond the scope of treatment. Drug therapy based on the British *Pharmacopoeia* is confusing.

One wonders why this book was published in America

where similar ground is well covered by books and monographs possessed by almost every physician.

Handbook of Bacteriology for Students and Practitioners of Medicine. By Joseph W. Bigger, M.D., Sc.D. (Dublin), F.R.C.P.I., M.R.C.P. (Lond.), D.P.H., M.R.I.A. Fifth edition. 8°, cloth, 466 pp., with 100 illustrations and 5 colored plates. Baltimore: William Wood & Co., 1939. $4.25.

The author originally set himself the task of writing a condensed textbook of bacteriology because of the frequent complaint of students that the majority of texts are too comprehensive for the usual course of three or four months' instruction. In this he has succeeded admirably. The essential and important phases of the entire subject are accurately presented and controversial matter is eliminated. The style is concise and clear. The present edition has brought this rapidly advancing science up to date, without appreciably increasing the length of the book.

This book should make an ideal text for elementary courses in medical bacteriology. It is not adequate as a reference book or text for advanced students, nor was this the intention of the author. It is regrettable that no references are given. The reviewer believes that a few well-chosen references are of value in guiding the interested and more ambitious student to additional reading—a habit which should be encouraged.

Climate and Evolution. By William Diller Matthew. Arranged by Edwin Harris Colbert. Preface by William King Gregory. With critical additions by the author and others and a bibliography of his scientific works by Charles Lewis Camp and Vertress Lawrence VanderHoof. Special Publications of the New York Academy of Sciences, Vol. 1. Second edition, revised and enlarged. 8°, cloth, 223 pp., with 33 illustrations and 5 tables. New York: New York Academy of Sciences, 1939. $2.00.

There is good occasion to rejoice at the appearance of the second edition, revised and enlarged, of Volume 1 in the series of special publications of the New York Academy of Sciences. The task of preparing this new edition was entrusted to Dr. Edwin Harris Colbert of the American Museum of Natural History, who has included many annotations found in Dr. Matthew's personal copy of *Climate and Evolution.* The preface contains, "A Biographical Sketch of William Diller Matthew, 1871–1930," an excerpt from an article in *Science* (1930) from the pen of Dr. William King Gregory. There is also an annotated bibliography of the author, covering twenty-two pages, arranged by Charles Lewis Camp and Vertress Lawrence VanderHoof.

All past and future readers should heed the following words from Dr. Gregory: "*Climate and Evolution* is one of those fortunate books that keep themselves alive. It deals with subjects of enduring scientific interest. And in our time all those who realize how fully the present state of the world is determined by its past history will value its clear statement of principles."

Principles of Development: A text in experimental embryology. Paul Weiss, Ph.D. 8°, cloth, 601 pp. New York: Henry Holt & Co., 1939. $5.00.

This volume embodies a discussion of problems in the field of experimental embryology. The text contains a critical account of the individual facts rated by the light they shed on these problems and the contributions they have made, or promise to make, toward their solution. The book is divided into four parts. The first, "The Phenomena of Development," considers the topics of growth, physicochemical changes, differential growth, differentiation, organization and the problems of development. The second, "The Methods of Studying Development," begins with a history of embryological methods, followed by a consideration of descriptive methods, experimental analysis and model experiments. The third, "Principles of Development," sets forth the problems of the initiation of development, preformed organization, progressing organization, gradual determination and the field concept, reintegration, regeneration and malformations. The fourth, "The Development of the Nervous System," discusses neurogenesis and concludes with a discussion of the development of behavior.

This book should prove very useful to teachers and students in the field of the biological sciences.

Laboratory Manual for Animal Histology. By Clair A. Hannum. 8°, paper, 105 pp., illustrated. Tucson: University of Arizona, 1939. $1.75.

This syllabus contains a simple account of cells, tissues and organs, with directions for studying prepared sections. There are twelve pages given over to a discussion of the technics for the preparation of tissues. The author gives several useful pedagogical suggestions in the section on microscopical anatomy.

Tumors of the Hands and Feet. Edited by George T. Pack, B.S., M.D., F.A.C.S. 4°, cloth, 138 pp., with 56 illustrations, and tables. St. Louis: C. V. Mosby Co., 1939. $3.00.

The recogntion and treatment of malignant growths present peculiar problems in the different regions of the body where they occur. The author has brought together in this text a complete review of tumors of the hands and feet. The introductory chapter deals with general principles, and it is followed by separate chapters on carcinoma, subungual melanoma, angiomatous tumors, synoviomas and tumors that are primary in the bones. These topics are authoritatively handled by the co-authors—Mason, Adair, Oughterson, Tennant, Brunschwig, Coley and Higinbotham. A work of this sort is designed more for the specialist than for the general practitioner; but it will serve to clarify the general surgeon's perplexities in conditions which he rarely sees, and to warn him of the dangers of lesions which might otherwise pass unrecognized or which may require more specialized judgment. Altogether, it is a very valuable addition to the literature.

Pictorial Midwifery: An atlas of midwifery for pupil midwives. By Sir Comyns Berkeley, M.A., M.C., M.D. (Cantab.), F.R.C.P. (Lond.), F.R.C.S. (Eng.), Hon. M.M.S.A., F.C.O.G. Third edition. 8°, cloth, 166 pp., with 245 illustrations. Baltimore: Williams & Wilkins Co., 1939. $3.00.

This book is exactly what it professes to be—an illustrated handbook designed to aid the midwife of Great Britain in her knowledge of the anatomy, physiology and pathology of pregnancy, labor and the puerperium. It is obvious that it should be a help to the pupil midwife in course or in preparation for state examinations, and also to the practicing midwife who desires to refresh her memory. The illustrations are well done, and the descriptive matter concise and simple. It is conceivable that the handbook could be useful to the medical student for use in conjunction with his textbook or as a rapid method of review of those subjects in which the information is satisfactorily transmitted by pictures. It also occurs to the reviewer that many of the illustrations would be useful in simplifying the teaching of nurses, as they clearly show what is now attempted in a series of didactic lectures.